S&T EXCELLENCE

Pan-European interdisciplinary Network for Attention Deficit Hyperactivity Disorder: Diagnosis, Treatment, Education

1.1.1. Description of the Challenge (Main Aim)

Attention Deficit Hyperactivity Disorder (ADHD) is the most common neurodevelopmental disorder in childhood and adolescence with a prevalence rate of 3-7% in Europe and worldwide, which according to population-based studies affects males at least twice as frequently as females. ADHD begins in childhood, with persistence of symptoms or the full-blown disorder into adulthood in up to 60%. The disorder is associated with adverse social, academic, economic, and emotional outcomes and poses a heavy burden on patients, families, and caregivers. While the evidence base for treatment of patients has grown significantly, both non-pharmacological and pharmacological treatment of children and adolescents differs substantially across Europe. This divergence in clinical practice including diagnostic aspects is rooted in differences with respect to socio-economic and cultural factors, but also reflects a lack of optimal education of parents, health-care professionals, educators, and the general public. Patients are thus treated sub-optimally or even put at a potential risk, thereby creating an urgent public health matter, with a dual impact on the health of youths and on health care budgets. Cost-effectiveness analyses of treatment strategies in ADHD have been initiated in several countries in Europe in an attempt to grasp and potentially curtail direct and indirect costs.

Short-to-mid-term benefits of stimulants such as methylphenidate (MPH), the mainstay of pharmacological treatment of ADHD in Europe, are well established. However, the absence of evidence for long-term effectiveness as well as concerns about potential risks associated with long-term stimulant use have entailed controversies within the medical field and beyond. The sheer number of exposed children, adolescents, and adults represents a significant public health concern. As a result, large scaled research efforts have recently been initiated in Europe and worldwide to assess the long-term safety of stimulants, particularly concerning central nervous and cardiovascular systems.

This COST Action will foster the creation of a pan-European, inter- and transdisciplinary scientific network to enhance evidence-based decision-making with a focus on physicians, psychologists, educators, and policy makers. As a result, the standards of care and education of professionals and the public will improve. A particular focus is on the assessment of diagnostic and treatment practices and school education of children with ADHD in all COST Member Countries. Efforts will entail delineation and integration of relevant socio-economic and socio-cultural issues, and will allow a critical reflection of the treatment strategies pursued in each European country. In light of the controversies related to medication treatment of ADHD we emphasize the need to understand divergent prescription rates and treatment regimens. In pursuit of academic and clinical excellence, a unique ADHD-Knowledge-Hub and a “Good Guideline Practice” (GGP) will be developed. The GGP will provide a tool for a quality controlled harmonization process regarding existing national guidelines and a template for the development of future guidelines for an up-to-date evidence-based treatment of ADHD in Europe and beyond.
1.1.2. Relevance and timeliness

High impairment: ADHD symptoms cause significant distress and impairment, and are pervasive (e.g. home, school). Associated with the disorder are reduced self-esteem, interpersonal relationship difficulties, elevated rates of accidents/injuries, comorbid mental and somatic disorders, reduced academic and occupational functioning, reduced overall and health-related quality of life (QoL), and elevated substance use and crime rates. Moreover, the negative impact of ADHD extends to family members with elevated rates of sick leave, divorce rates, and reduced QoL. Current treatment practice is suboptimal. High rates of impairment persist, which may be due to too little, too much or ineffective treatment.

Gender effects and lower academic achievement: The traditional focus on the academic achievements of girls has partially reverted to concerns about the perceived underachievement of males (“crisis of masculinity”), who are more frequently affected by ADHD. This disorder is associated with poor grades, increased grade retention, increased use of school-based services, elevated rates of detention and expulsion, and ultimately with lower rates of high school graduation and postsecondary education. In the short-term, ADHD medications have some potential to reduce the negative impact of the disorder, but the magnitude of these improvements is often small. Critically, standardized test scores and ultimate educational attainment are not improved by medication in the longer term.

Concerns about potential over- or underdiagnoses: A key question for health care professionals, health insurance, and policy makers is whether DSM (Diagnostic and Statistical Manual of Mental Disorders) over-identifies or ICD (International Classification of Diseases) under-identifies ADHD. A recent meta-analysis of 175 studies based on DSM-III, DSM-III-R, or DSM-IV criteria for childhood ADHD revealed a pooled benchmark prevalence estimate of 7.2%, while estimates of 3-5% have been obtained in studies based on ICD-9 and ICD-10. Apart from the use of different sets of diagnostic criteria, the divergent prevalence rates may be explained by differences in impairment criteria, sample sizes, and assessment procedures (e.g. ratings by patients, parents, teachers, clinicians). Upon adjustment for study methods, prevalence estimates did not vary as a function of geographical location or year of study during the past three decades.

Large economic impact: ADHD places a significant economic burden on multiple public sectors; the majority of the societal costs of this disorder are generated outside of the health care system. Based on data of six northern European countries, societal costs of minors with ADHD have been estimated at approximately €1 billion annually for a population of 16 million, the largest cost category being education (€648 M). Societal costs for children with ADHD in Europe were estimated to amount to €1173 for direct annual medical costs per patient compared to €177 for children without ADHD. Annual indirect costs for mothers of a child with ADHD due to absence from work were estimated at €2243 compared to €408 for other mothers.

Timeliness: The initiation of this European dialogue is urgently required to optimize education and evidence-based treatment of children and adolescents with ADHD and to facilitate the work of their caregivers: Patients and their families should have access to best practice in all COST Member Countries and beyond. The COST Action will serve as a model well beyond Europe. The identification of the socio-economic and socio-cultural factors underlying national differences will enable patients, parents, their clinicians/therapists, and patient groups to critically reflect on the diagnostic and treatment modalities within their country. Information about the effectiveness of particular forms of schooling with respect to academic achievement and social and emotional development of children with ADHD is of obvious importance for parents, educators, and policy makers, to enable optimal educational services and/or impinge on educational professionals and politicians. Health care professionals need to be informed about the evidence base important for his/her work, as well as about the boundaries of the evidence and additional/alternative treatment strategies. A ‘common language’ is required to enable the best “interdisciplinary” treatment for each individual child seeking specialized help.

A lack of consensus between investigators on how to best ascertain the disorder may drive overt prevalence and prescription rates, which is not in the interest of policy stakeholders. Reasons...
underlying divergent rates in prescription and use of stimulants require explanation to allow a national health care system to adjust if deemed necessary. In the UK stimulant prescriptions rose 96-fold between 1992 and 2001\textsuperscript{10}. In Germany prescriptions of MPH increased 187-fold between 1990 and 2009\textsuperscript{11}. MPH use has reached the top of prescriptions dispensed to adolescents according to several recent national reports\textsuperscript{12-14}. Substantial prescription increments over the past 25 years, which have begun to plateau in individual countries, entail serious questions as to the long-term efficacy and safety of these drugs, particularly for children\textsuperscript{15,16}. Whereas short- and medium-term side effects have been investigated thoroughly\textsuperscript{3,4,17-19}, the potential long-term effects are difficult to investigate and as such constitute a matter of substantial debate. Currently, there is little evidence to indicate that stimulants have a positive effect after a period of two or more years\textsuperscript{20-22}. Because of the high rate of exposed subjects, even infrequent and/or minor long-term side effects could have a serious impact on public health. Regulations for the prescription of stimulants differ across Europe\textsuperscript{23}, the effects of which should be explored both in the context of stimulant use by children and adolescents, and abuse in adolescents and adults; the latter is seemingly increasing across Europe\textsuperscript{24}. The emergence of novel non-pharmacological modes of treatment requires critical evaluations of effectiveness and safety, to justify the respective costs of service provision. Accordingly, policy makers, funding agencies and regulatory authorities require input to steer implementation of non-pharmacological treatments.

The steeply increasing number of publications on ADHD (PubMed for 2000, 2010, and 2014: 631, 1981, and 2704, resp.) entails the difficulty to keep abreast of novel developments. Accordingly, national guideline groups are finding it increasingly difficult to update their work. Existing national guidelines have not been updated in recent years, while other countries do not have the resources for guideline development at all. The European Guideline for Children and Adolescents was published by the European Society of Child and Adolescent Psychiatry (ESCAP) in 2004 and supplemented in 2006. Thus, while welcome, the ever increasing knowledge base comes with a challenge to attain a holistic perspective on ADHD, thus requiring a pan-European, inter- and transdisciplinary scientific network.

1.2. Objectives

1.2.1. Research Coordination Objectives

This COST Action pursues the pan-European, interdisciplinary coordination of ADHD related clinical and teaching practices, and of existing research activities funded either at local, regional, national or European levels. The Action involves both Early Career Investigators (ECI) and renowned Senior Experts (SE) with backgrounds in child and adolescent psychiatry, paediatrics, cardiology, pharmacology, education, psychology, biology, biometrics and biostatistics, epidemiology, sociology, and health economy to promote an interdisciplinary approach towards children/adolescents with ADHD. The Action allies with existing high quality European scientific communities, projects, organisations and patient groups.

The main objectives include:

- Compilation of identically structured data sets for each participating COST Member Country, COST Cooperator State, and COST Near Neighbour Country allowing cross-country comparisons of clinical practice, education, and research activities
- Coordination of goal oriented meetings involving ECI and SE with a track record in ADHD research and/or policy issues, to analyse the cross country data sets and to draw conclusions regarding the optimisation of clinical practice, education, and research strategies
- Development of a “Good Guideline Practice” (GGP) to foster harmonization of clinical practice guidelines via a process of consensus finding
1.2.2. Capacity-building Objectives

- The creation of an ADHD-Knowledge-Hub based on the compilation of the national data to enhance broad dissemination of the results of cross-country comparisons, with the goal of stimulating best practice, research, and interdisciplinary cooperation.
- Realization of an interdisciplinary and holistic approach to tackle the Challenge (see 1.1.1.) through the inclusion of diverse professions.
- Broad dissemination of the GGP via coordination of stakeholder meetings (guideline committees, patient associations, insurance companies, regulators, policy makers, pharmaceutical companies) in which the GGP will be presented as a tool for a quality controlled harmonization process.
- The COST Action will support policy stakeholders of national health care systems to evaluate the compatibility of their policies with the current evidence base. It is crucial that cost-effective and safe treatments are propagated, while ineffective, costly and potentially unsafe treatments are discouraged.
- ECI from Cost Member and especially Inclusiveness Target Countries, but also COST Cooperating States, and COST Near Neighbour Countries are invited to collaborate, thereby substantially increasing their knowledge base both within and beyond their respective fields, thus enhancing their professional decisions, their research, and their career options through network contacts established by this Action.

1.3. Progress beyond the state-of-the-art and Innovation Potential

1.3.1. Description of the state-of-the-art

The exact etiology of ADHD is still unknown. A major issue is the large heterogeneity among ADHD patients with potentially different aetiologies, differences in clinical symptomatology and severity, as well as in comorbidities. Current aetiological hypotheses include a dysbalance in the signalling of monoaminergic neurotransmitters and a hypofunction in frontal-striatal circuitries. Volumetric reductions of the basal ganglia and cortical thinning have been reported. ADHD has been shown to be highly heritable. Like in other psychiatric disorders, a multifactorial basis including a polygenic predisposition accounts for the development of the disorder; genetic loci with genome wide significance have not yet been identified. However, an overlap of genetic risk factors with other psychiatric disorders appears likely. Prenatal (e.g. in utero exposure to alcohol), perinatal, and postnatal environmental factors contribute to the aetiology and the severity of symptoms. To date there is neither a biomarker for ADHD itself nor for the response to stimulant medication.

Clinical practice: Because the psychiatric nosology for ADHD will continue to be based on clinical assessment of symptoms, this COST Action is crucial to support standardizing diagnostic assessments and treatments. Existing European guidelines refer to DSM-IV or ICD-10 and need to be updated with regard to DSM-5 and ICD-11 criteria. National guidelines lag behind more recent developments (see “1.1.2 Relevance and timeliness”). Reasons for the enormous rise in prescription rates are unknown, as is the adherence to stimulant treatment guidelines across Europe. The concern on possible overtreatment is opinion-based rather than evidence-based, and actual rates are sorely lacking. Apart from possible overtreatment due to over-diagnosis, the increased rates of medicated children and adolescents may be explained by better recognition of ADHD, in particular among girls, and longer treatment duration. The increased and longer use of stimulants contrasts with the lack of long-term data on effectiveness. The Multimodal Treatment of ADHD study found that children taking stimulants alone or combined with behavioural treatment fared better in the first year compared to children who received no special care or who received behavioural treatment alone. Later, long-term reports after eight years found those still taking stimulant medication fared no better in the reduction of symptoms or in social functioning than those who had stopped medication. An important omission of the present practice guidelines is the lack of specific criteria when to discontinue stimulants.
Non-pharmacological interventions, including dietary (restricted elimination diets, artificial food colour exclusions, and free fatty acid supplementation) and psychological (psycho-education, parent training, cognitive training, neurofeedback, and other behavioural interventions) treatment options have been shown to result in significant albeit small effects, if raters were close to the therapeutic setting. However, a more rigorous analysis based on e.g. blinding of objective raters found limited evidence for free fatty acid supplementation and artificial food colour exclusion⁴³.

**Educational aspects:** Research evidence shows that teachers who are effective in supporting students with ADHD are proactive in creating positive relationships with their students and are able to promote prosocial relationships among students⁴⁴. They are also able to use their understanding of ADHD and related conditions to adapt their pedagogy and create an ‘ADHD-Friendly’ environment. They are skilled in positive group behaviour management, and utilize behavioural and cognitive behavioural⁴⁵ approaches at both group and individual levels. Evidence also shows the efficacy of certain pedagogical adjustments⁴⁴. Owing to the complex nature of ADHD it is often important for schools to engage with students’ parents and in trans-professional relationships with health and mental health professionals and others, such as social workers.

### 1.3.2. Progress beyond the state-of-the-art

This Action will increment the current state-of-the-art by:

- Building-up of a novel interdisciplinary data- and knowledge-base embedded in the ADHD Knowledge Hub. This know-how will be made accessible in a target-group-specific manner to all interested in, affected by, or professionally dealing with ADHD. Importantly, socio-cultural and socio-economic factors potentially influencing ADHD treatment in COST Member Countries will be analysed for the first time, thus allowing a critical evaluation of current national practices and the crystallisation of an over-arching approach to best practice
- Focussing on an interdisciplinary and holistic approach towards children and adolescents with ADHD; the inclusion of professionals from different fields entails that factors relevant in education of children with ADHD will be viewed side by side with those of the medical/ psychological/psychotherapeutic fields; the inclusion of socio-cultural and economic aspects will further broaden the perspective
- Creating unprecedented intellectual capacity on a goal oriented ADHD centred research agenda by connecting high-quality researchers and scientific communities, and involving ECI throughout all processes
- Supplying national guideline committees with a unique GGP as a tool to facilitate harmonization processes and potentially lead to new treatment concepts in the COST Member Countries
- Increasing awareness of both the necessity for and the impact of evidence based research

### 1.3.3. Innovation in tackling the challenge

- This COST Action makes maximal and systematic use of the analysis of current divergences in COST Member Countries to foster the development of an overarching best practice approach
- The formation and technical realization of an ADHD Knowledge Hub is one of the major innovative, tangible deliverables of the Action. Because research funding of fields with a focus on paediatric ADHD is not readily available in most of the COST Member and Inclusiveness Target Countries, the Action guarantees the participation of many ECI and SE who are motivated to contribute to the Action in key positions (3.1.1)
- The GGP is a unique, tangible and innovative solution for the harmonization of clinical treatment guidelines for ADHD and a generic best practice instrument and template; the GGP will reach out internationally and beyond the scope of this Action
- This COST Action will in many ways pave the way for other childhood mental disorders with respect to the interdisciplinary and holistic approach. Moreover, this COST Action will shape fundamental decision-making processes required for initiation/discontinuation of pharmacological and/or non-pharmacological treatment
1.4. **Added value of networking**

1.4.1. **In relation to the Challenge**

Mutually beneficial cooperation between SE and ECI as the major **driver of networking** is an innovative concept boosting collaboration across COST Member Countries and beyond. For this purpose this COST Action will form thematic core units of SE and ECI in all Working groups (see 3.1.1.) A direct dissemination through existing national and international scientific information channels and communities is warranted. The interdisciplinary network will enable delineation, evaluation and dissemination of findings regarding European diversity of ADHD related clinical practice and education. **Exchanges/collaborations** will be sought with **policy makers, regulatory agencies, insurance companies, patient organizations, and the pharmaceutical industry.** This Action will be supported by existing European networks and scientific societies (see 1.4.2).

1.4.2. **In relation to existing efforts at European and/or international level**

This Action does not overlap with any current or planned European research project. It is however, highly **complementary** to the largest initiatives that are currently operative for the study of ADHD at the European level. Examples include **ADDUCE** (Attention Deficit Hyperactivity Drugs Use Chronic Effects), but also the European Network for Hyperkinetic Disorders (EUNETHYDIS), and it’s subdivision the European ADHD Guidelines Group (EAGG), Dutch Knowledge Centre, European Society of Child and Adolescent Psychiatry (ESCAP), European College of Neuropsychopharmacology (ECNP), International Multisite ADHD Genetics (IMAGE) project, and Enhancing Neuro Imaging Genetics through Meta-Analysis (ENIGMA) project. The Action aspires to expand into a **global initiative**, reaching investigators from Europe, Africa, America, Asia, and Australia. Finally, interactions with other **international initiatives** on ADHD will be implemented through the variety of outreach activities carried out throughout the Action, such as an **open international conference, annual training workshops** organized by each of the working groups, and the participation of experts of this Action in **international conferences**.

**IMPACT**

2.1. **Expected Impact**

2.1.1. **Short-term and long-term scientific, technological, and/or socioeconomic impacts**

This network of European experts **bridges** different research communities, disciplines, fields and methodologies and lines up with patient/parent associations and policy makers, who will all join efforts to increase our understanding of ADHD, and to optimize the diagnosis, treatment, and education of children with ADHD. The interdisciplinary and holistic approach has the potential for substantial research **spin-offs**. It is crucial to identify the factors underlying European diversity **including socio-economic and frequently neglected socio-cultural factors**. The knowledge base that will be gathered in a database and disseminated via a website and publications will offer interested parties access to relevant information, thus providing guidance as to future research ventures. Cross-country comparison will allow critical reflection of national practices, resulting in a significant increase of the standard of care for individuals with ADHD across Europe. The **Action Website** will act as an important source of information for all stakeholder including individuals with ADHD, their parents and teachers. At the same time, the **outreach activities** of the project, targeting the general public, educators, and policy makers, will increase public awareness about the disorder, **combat stigmatisation and discrimination** against patients with ADHD, thus leading to **inclusion activities and improving their QoL**. In addition, this Action extends beyond the benefit of new knowledge on ADHD, as it will **provide a model for other mental/behavioural disorders**. This Action will undoubtedly **improve and streamline harmonization processes**.
related to other childhood onset mental disorders and yield a sustainable social impact and fiscal benefit across Europe.

So far treatment cost-effectiveness studies have primarily focused on MPH, which came out as a cost-effective treatment option\textsuperscript{17}. The Action will evaluate how cost effectiveness calculations of MPH are affected by under- or over-diagnosis of ADHD and respective under- or overtreatment, in order to propose solid overall cost impact estimates and improvements. Even small shifts in the prevalence and treatment of ADHD could have important fiscal implications for institutions involved in the treatment of ADHD\textsuperscript{5}.

One core vision of this Action is to enable the development of one globally applicable guideline template [GGP] (comparable to global guidelines and recommendations as e.g. CONSORT (CONsolidated Standards of Reporting Trials)\textsuperscript{48} or PRISMA (Preferred Reporting Items for Systematic Review and Meta-Analyses)\textsuperscript{49}). The realization of this template would set free energy and resources that are currently bound by the redundant evaluation of the scientific evidence for the development and update of national guidelines.

2.2. Measures to Maximise Impact

2.2.1. Plan for involving the most relevant stakeholders

The Action participants will ally with ESCAP and form an alliance with ADDUCE, Eunethydis, EAGG, and ECNP. Patient organisations, policy makers and other target groups (see 2.2.2) will be addressed directly via invitations to participate in activities of the Action (training courses, seminars, conference, roundtable discussions) and indirectly through the COST Action Website.

2.2.2. Dissemination and/or Exploitation Plan

This Action will create a dynamic pan-European integrated platform, aiming to consolidate existing knowledge and to facilitate harmonisation of strategies regarding diagnosis, treatment, and education of individuals with ADHD throughout Europe. The activities of this Action will be disseminated as widely as possible:

The target groups are:
- ECI and SE, either clinical or basic scientists
- Clinicians involved in the diagnosis and treatment of ADHD
- Educators (education researcher and teachers in primary and secondary education)
- European and national policy makers
- Regulatory authorities
- Pharmaceutical industries
- Insurance companies
- Individuals with ADHD and their families
- Patient/parent associations
- The general public

Methods of dissemination include:
- Research seminars and training courses
- Round tables in national, European, and international conferences
- An international conference on the diagnosis and treatment of ADHD incl. public day
- Publications in peer reviewed scientific journals
- Compilation and distribution of educational material to educators and medical professionals
- Participation in delineation and contribution to publication of guidelines (in collaboration with EAGG)
- Lecture Series on ADHD from different perspectives
- Central project website and weblogs
Implementation: Dissemination of results represents a core task in this COST Action. The overarching Working Group “Knowledge Hub and Outreach Activities” (WG3) will design, coordinate, and implement all outreach and dissemination activities including the setup of the interactive Action website. Aims, planned activities, and results of the Cost Action will be made publicly available, and will include scientific reports, social and economic impact analyses, a guideline template, and draft guidelines on ADHD diagnosis, clinical assessment and multi-modal treatment. Translations of any type of information will be encouraged; we will attempt to identify at least one expert in every participating country, who is committed to participate in weblogs that will serve as discussion forums among scientists and patients in the respective language. The Action will have an important impact in raising public awareness, and will educate teachers and influence the school environment of children with ADHD. The Action will proactively invite (posted on the website) investigators and will be open for other interested parties to join. Goal-oriented workshops and training seminars will be organised by each of the WGs and will be open to researchers and clinicians from Europe and beyond. For the duration of the Action, roundtables on different aspects of ADHD research will be organised at major scientific conferences. Finally an inspiring international conference will be organized regarding the harmonization of current practices for the treatment of ADHD, with a particular focus on socio-cultural and –economic factors underlying divergence, which will be open to health care providers, scientists, educators, politicians, industry representatives, patients, families, and patient organizations.

2.3. Potential for Innovation versus Risk Level

2.3.1. Potential for scientific, technological and/or socioeconomic innovation breakthroughs

The development of a “Good Guideline Practice” throughout this Action is an innovative step forward and follows so-called “best GxP traditions”. The GGP shall streamline the drafting of new, respectively support the updating of existing, national and European guidelines, focusing on socio-economic factors, socio-cultural factors, and long-term clinical management, thus extending current guideline contents. The GGP will ease future harmonization approaches on a European and international level with an impact far beyond this Action. Starting with an Action Website, the novel interdisciplinary data- and knowledge-base embedded in the ADHD Knowledge Hub will be developed in the course of the Action. The respective work will be performed within the core units comprised of ECI and SE. To support this work and to minimize the risk level with regard to the financing of the ADHD Knowledge Hub, Action participants will use already existing funding sources and submit grant applications also with the aim to warrant sustainability beyond the Action.

ECI (the majority of who are females) will be provided with unique opportunities to structure part of their own future careers, to prudently pursue best practices in their respective fields, and to become highly respected opinion leaders of tomorrow. This Action offers the unique opportunity to clarify clinical, research, ethical, and policy issues related to medication of children and adolescents with mental disorders. ECI, from the Inclusiveness Target Countries who cannot readily obtain research funding, will have the unique opportunity to engage in research under the supervision of experienced scientists. Action participants have proven experiences in international networks and societies (e.g. ESCAP involving 27 countries) with educational components and in depth knowledge of training and education concepts.
3.1. Description of the Work Plan

The objectives (see 1.2.1 and 1.2.2) will be pursued through three inter-related Working Groups (WG). **WG1-Data-Mining and Analysis** will start with 1) precise delineation of the variables of interest to be subjected to a cross-country comparison, followed by 2) fixation of the respective methodologies (e.g. surveys, questionnaires, interviews, online searches, and/or official requests addressed to government and other sources) and 3) data collection. 4) Data analysis concepts will be developed in collaboration with **WG3-ADHD-Knowledge-Hub and Outreach Activities**, which will be responsible for setting up the database. Finally, **WG1** will 5) pursue all data analysis tasks and 6) create a consensus picture, which will impact the tasks of **WG2-GGP Development and Harmonization**. **WG2** will 1) evaluate existing EU and national guidelines, 2) align with stakeholders from guideline committees, and 3) develop a best practice concept finally resulting in the GGP. **WG2** will closely interact with **WG1** for the integration of their results and with **WG3** for all dissemination and outreach activities. **WG3** will work as a knowledge-base whose tasks will involve 1) the creation of a database for **WG1**, 2) organization of the ADHD-Knowledge-Hub infrastructure, 3) organization of meetings, courses, and conferences, and 4) creation of a dissemination platform. All activities require **intensive collaboration, frequent meetings, supervision by the management teams** (see 3.2), and **reporting/publication** of the results.

3.1.1. Description of Working Groups

**WG1 Data-Mining and Analysis**: The major task consists of **data compilation and analysis to allow determination and evaluation of the status quo regarding treatment** for children and adolescents with ADHD for every participating country, while allowing the integration of data sets of other countries. **WG1** will perform the cross-country analyses using appropriate statistical methodology and evaluate the results to deduct best practice principles whenever meaningful and appropriate. These central tasks will be pursued within distinct taskforces (e.g., diagnostic issues, pharmacological and non-pharmacological treatments, education and teaching, socio-cultural and socio-economic factors, and cost-effectiveness), consisting of both ECI and SE with an expertise in the specific research field. Whereas the work laid out in this work group requires mainly meetings, funding of knowledgeable statisticians may be required for specific complex analyses. The central tasks for this WG are:

- Data compilation - to be accomplished via **Short Term Scientific Missions** - based on identically structured data protocols to enable trans-European comparisons of:
  - ADHD diagnosis rates in children and adolescents sub grouped according to sex and age
  - Clinical practice regarding pharmacological treatment initiation and long-term follow-up
  - Clinical practice regarding non-pharmacological modes of treatment
  - Factors potentially influencing treatment strategies at the national level (e.g. socio-economic and socio-cultural factors, national guidelines, regulations for the prescription of ADHD medications in different age groups, national mental healthcare budgets, ADHD related activities of the pharmaceutical industry, training regarding ADHD for health care professionals
  - Educational factors in primary and secondary education potentially relevant in ADHD (e.g. predominant teaching methods, average number of pupils per class, number of teachers, education of teachers with respect to ADHD, perception of the relevance of ADHD for daily work and of the strain imposed on teachers by children with ADHD, special educational programs for children/adolescents with ADHD)
  - National health, educational, and societal costs for ADHD in minors
  - Research programs funded by national agencies
  - National lists of clinical scientists, educators, opinion leaders, patient association groups policy makers, representatives of the pharmaceutical industry, journalists, and other relevant professionals with an interest in the activities and deliverables of this COST action

- Design of the analysis (e.g. generation of appropriate hypotheses, selection of statistical methods, delineation of the required infrastructure, assignment of Short Term Scientific Missions to particular researchers, after approval by the MC see 3.2).
- Conductance of the cross-country analysis (Short Term Scientific Mission) based on the compiled national data sets
- Discussion and interpretation of the results, allowing conclusions as to best practice approaches, writing reports and scientific publications

WG2 GGP Development and Harmonization will coordinate with WG1 in order to define the overarching topics required for GGP development:
- Development of a “Good Guideline Practice” (GGP) via a process of consensus finding between renowned SE and ECI (see Capacity-building objectives 1.2.2.):
  - Delineation of ethical guidelines and appropriate declaration of conflicts of interest for participants of all WGs under consideration of this ambitious initiative, its interface with appropriate regulatory bodies, and the pharmaceutical industry
  - Alliance with existing experts and existing consortia for the development of so-called “must have” criteria for treatment guidelines
  - Development of a multilingual template for guidelines
  - Provision of scientific support to coordinate the multilingual translation and validation of guideline relevant clinical instruments in partner countries that are currently lacking such tools
  - Coordination of initiatives to align with national and European guideline committees for implementation of the GGP, fostering harmonization of clinical treatment practices across COST Member Countries and beyond
  - Collaboration with EAGG including provision of relevant outputs of WG1 & 2 to stimulate updating of guidelines for ADHD diagnosis, clinical assessment, and treatment at European and national levels
  - Organisation of training courses, allowing medical professionals to benefit from a comparison of their own practice with that of established clinics/hospitals specialized in the assessment and management of ADHD and related disorders

WG3 ADHD-Knowledge-Hub and Outreach Activities: This WG will design and coordinate the implementation of all database, outreach and dissemination activities, thereby having an overarching purpose towards achieving the aims of this COST Action. For the sake of sustainable information storage and access to the tangible results of this COST Action, a state-of-the-art ADHD-Knowledge-Hub will be created with the option for a multitude of interactions and outreach activities, including a virtually permanent expert forum. This WG will receive input from investigators and tasks completed in WG1 – 2:
- Creation of the Action website (core element of ADHD-Knowledge-Hub) with state-of-the-art science regarding diagnostic measures and ADHD treatment efficacy and safety. Information will be provided for patients and their family members, teachers, health care professionals, policy makers, and the interested lay public. The COST Action will strive to make this information available in as many languages as possible
- Development of protocols to guarantee security of stored data
- Development of guidelines for data access and sharing
- Preparation and submission of grant proposals to national, European, and international funding agencies, in order to ensure the advancement and uninterrupted maintenance of the database and transform it in a sustainable ADHD-Knowledge-Hub
- Creation of a weblog that will enable the communication among patients, families, and national associations of ADHD individuals
- Identification and selection of at least 50 clinical, scientific, education, and policy experts (child and adolescent psychiatrists, epidemiologists, educators, teachers, public health experts, pharmacologists, cardiologists, neurologists, sociologists) willing to hold state-of-the-art
These lectures and discussions will be accessible to all interested parties in COST Member Countries and beyond. Coordination of goal-oriented meetings, training sessions, and annual research seminars involving both ECI and SE with a track record in ADHD research and/or policy issues. Organisation of an international conference on ADHD, which will be open to researchers, as well as patients and their families. Development and distribution of educational material to educators and medical professionals. Commencement of dialogue with policy makers on the issues of public awareness for ADHD. Dissemination activities will also include the publication of articles in the native language of participating countries (both in scientific journals, as well as the project website), aiming to provide information accessible to the general public. Importantly, this WG will organise events (e.g., round-tables) that target stakeholders, policy makers, educators, and the general public, and aim to raise public awareness about the disorder, combat stigmatisation of and discrimination against individuals with ADHD and improve their quality of life.

3.1.2. GANTT Diagram

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<th>Activities and milestones</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
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<tr>
<td>Kick-off Meeting</td>
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<td>Report first results at intl. conferences</td>
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<td>Stakeholder dialogues</td>
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<td>State-of the art meeting, all WGs</td>
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3.1.3. Risk and Contingency Plans

The planned activities of this Action entail costs, not covered by the budget of the Action, such as the development and maintenance of the ADHD-Knowledge-Hub. The risk mitigation plan foresees to start with the Action Website as a core element and search for additional funding sources for the creation of this unique knowledge base (finally via grant applications and/or associations with existing European projects or European Societies).

Any COST Action entails risks related to a lack of participation, drop-out during the course of the Action, and difficulties regarding networking. Risk and contingency mitigation is plausible, based on the strong integration and prominent roles of participants in very active European Societies and the successfully proven experience in very large European and international projects and consortia.

3.2. Management structures and procedures

The management structure of this COST Action includes the following actors: A Chair and a Vice-Chair, both elected, who preside over the Management Committee (MC). The MC oversees the work of the four Working Groups, each of which is managed by a Coordinator and Co-Coordinator. The members of this Action will have a special focus on gender aspects with regard to participation and leadership in teams, and encourage female experts to candidate for leadership positions. Together with the Chair and Vice-Chair, WG Coordinators and Co-Coordinators form the Steering Committee (SC). The MC will be appointed to oversee and coordinate the key issues of the programme. It will consist of up to two representatives per participating country, including the Coordinator and Co-Coordinator of each WG. The MC will meet once a year for the duration of the project and will remain in continuous contact through the use of web-based interfaces. The MC will oversee the allocation of funds, and will be responsible for the overall strategy of the Action. It will be responsible for the management of the Action, appointing the WGs that will implement the Action and continuously monitoring their progress. The MC will also be responsible for the establishment of contacts with other European and international programmes, associations, and governmental bodies. Finally, the MC will prepare reports related to the Action, organise the preparation and submission of a proposal for a large-scale Horizon2020 project.

The SC will constitute a more flexible instrument that will allow the close monitoring of the progress of the Action, acting as a liaison between the different WGs and participating in key meetings of the WGs. Under the directions of the MC, the SC will oversee the management and evaluation of the Action. The SC will meet once or twice a year and will communicate through the use of web-based interfaces and regular conference-calls. The Coordinator of WG3 will also act as Dissemination Manager and nominate a Website Manager searching approval from the COST-Chair and MC. The COST-Chair shall also act as the ECI-Manager to underline the importance of ECI as key contributors to this Action.

The most important milestones of this Action will be the following:

- Two day kick-off meeting at the start of the Action, with the participation of all members of the MC. The meeting will be advertised and will be open to all investigators from COST Member Countries interested to participate.
- Creation of the Action website (WG3) which will be developed towards the ADHD-Knowledge-Hub. The project website will serve as a forum for communication among network members, and importantly with policy makers, other stakeholders, and the general public.
- Creation of ADHD related weblogs targeting general audiences (families, patients and teachers) as well as researchers.
- Support of the Development of harmonized and updated guidelines for the clinical assessment and treatment for ADHD by means of the GGP.
- Annual thematic training workshops for ECI, organized by each WG.
■ STSMs for ECI and SE and full integration of ECI in leading positions, as recommended by individual WGs and the MC.
■ Submission of a grant application.
■ International conference including a public day in the fourth year of the Action.

3.3. Network as a whole

At the European level it is crucial to add socio-cultural and socio-economic perspectives to clinical and scientific research. Furthermore there is an urgent need to enable ECI of all participating countries to directly profit from the respective research results and to ensure maximal dissemination to health care professionals, patients, their parents and teachers. Young members of research academies and relevant expert associations (see above) will work together with experts from multiple disciplines. Various patients/parents associations will actively be included to construct a powerful base for successful pursuance of this COST Action. The link to European key opinion leaders and stake holders is guaranteed as well as the participation of representatives of most likely all European member states. Ambitions of Early Career Investigators will be maximized during challenging exchanges with experts, and through publication and networking opportunities. Senior investigators are responsible for the supervision of the study design, data collection, discussion and publication of such studies. A great advantage of this COST Action is the provision of an access and integration of male and female researchers from Inclusiveness Target Countries.

REFERENCES

deficit/hyperactivity disorder.


