

Brussels, 24 March 2020

COST 018/20

DECISION

Subject: **Memorandum of Understanding for the implementation of the COST Action
“Network for blood pressure research in children and adolescents”
(HyperChildNET) CA19115**

The COST Member Countries and/or the COST Cooperating State will find attached the Memorandum of Understanding for the COST Action Network for blood pressure research in children and adolescents approved by the Committee of Senior Officials through written procedure on 24 March 2020.



MEMORANDUM OF UNDERSTANDING

For the implementation of a COST Action designated as

COST Action CA19115
NETWORK FOR BLOOD PRESSURE RESEARCH IN CHILDREN AND ADOLESCENTS
(HyperChildNET)

The COST Member Countries and/or the COST Cooperating State, accepting 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 (the 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 new document amending or replacing them:

- a. "Rules for Participation in and Implementation of COST Activities" (COST 132/14 REV2);
- b. "COST Action Proposal Submission, Evaluation, Selection and Approval" (COST 133/14 REV);
- c. "COST Action Management, Monitoring and Final Assessment" (COST 134/14 REV2);
- d. "COST International Cooperation and Specific Organisations Participation" (COST 135/14 REV).

The main aim and objective of the Action is to establish a European sustainable and multidisciplinary network focusing on acquiring a holistic understanding of the factors affecting high blood pressure in children and adolescents in order to propose and implement corrective and preventive actions both globally and locally.. This will be achieved through the specific objectives detailed in the Technical Annex.

The economic dimension of the activities carried out under the Action has been estimated, on the basis of information available during the planning of the Action, at EUR 80 million in 2019.

The MoU will enter into force once at least seven (7) COST Member Countries and/or COST Cooperating State have accepted it, and the corresponding Management Committee Members have been appointed, as described in the CSO Decision COST 134/14 REV2.

The COST Action will start from the date of the first Management Committee meeting and shall be implemented for a period of four (4) years, unless an extension is approved by the CSO following the procedure described in the CSO Decision COST 134/14 REV2.

OVERVIEW

Summary

Hypertension (HTN) is now responsible for 7.1 million deaths per year worldwide, and largely contributes to cardiovascular and renal diseases such as ischemic heart disease, stroke and chronic kidney disease. Cardiovascular and renal diseases linked to high blood pressure (BP) are the first cause of mortality in Europe with an economic impact cost of approximately 1 billion euros per year. In fact, although most of the adverse outcomes occur in adulthood it has become clear that high BP is a life course problem that can become evident in early life.

While few would dispute the importance of taking effective steps to identify and manage this condition in middle-aged and older people, relatively little attention has been paid to the problem of high BP in children and adolescents.

As a consequence, despite the latest advances and the wide literature on BP in children and adolescents, the solutions to relevant questions are still pending. Thus, scientific and clinical community, as well as decision-makers, stakeholders and the overall society, must face some critical problems related to the high BP in children and adolescents as a cardiovascular risk factor.

The COST Action **HyperChildNET** is aimed at establishing a European sustainable and multidisciplinary network of internationally renowned researchers, clinicians, early career investigators, health economists, decision-makers, patients, regulatory bodies, nutrition & pharma companies and medical devices manufacturers focusing on acquiring a holistic understanding of the factors affecting high BP in children in order to propose and implement corrective and preventive actions both globally and locally.

<p>Areas of Expertise Relevant for the Action</p> <ul style="list-style-type: none"> ● Clinical medicine: Paediatrics 	<p>Keywords</p> <ul style="list-style-type: none"> ● blood pressure ● children and adolescents ● origin, impact and prevention of high blood pressure ● clinical guidelines, policies and action plans for high BP
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Specific Objectives

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

Research Coordination

- To benchmark, assess and select suitable devices for office BP monitoring in children and adolescents that fulfil the overall criteria of the universally acceptable standard (AAMI/ESH/ISO).
- To define reference values for BP that can be applied all over Europe. This will be cornerstone for the definition of uniform criteria that allow a better stratification and follow-up of HTN in children. This is also the starting point for a better definition of BP categories.
- To define the best methodological approach for the European clinical and research community to assess hypertension-induced organ damage.
- To produce guides, publications and ICT-based tools to prevent high BP in children and adolescents taking into account different confounding factors (obesity, physical activity, eating patterns, smoking, social and psychological factors, family communication skills) for a wide range of target groups.
- To assess the economic impact of recommended policies and stakeholders' intervention.

Capacity Building

- To promote Workshops, Conferences, Short Term Scientific Missions (STSMs) and Training Schools (HyperChildNET Academy), for knowledge-exchange focusing on a topic of clear scientific and socio-economic application through joint actions.
- To enable the sharing of best clinical practice and scientific state-of-the-art within a European context, which will also sustainably improve collaboration. This will be achieved through Training Schools (HyperChildNET Academy) and capacity building for Early Career Investigators (ECIs).
- To adopt an interdisciplinary approach to the research agenda by involving medical practitioners, nurses, policy makers, medical device OEM and scientists in the Action, as required for successful adoption of best practices and cross-national cooperation. The HyperChildNET Ecosystem of Stakeholders locally and internationally will be created for this purpose.
- To promote the sustainability of the network beyond the life of the Action by encouraging network members to develop collaborative funding applications, continuing the liaison established among researchers after the duration of the Action and maintaining the planned website as a sustained open resource.
- To foster international cooperation between researchers from COST member countries, COST Near Neighbour Countries (NNC) and International Partner countries (IPC), bringing together different disciplines to enable breakthrough scientific developments in this field of research.
- To increase the overall awareness of the importance of high BP along childhood, and how to halt the growing epidemic of related factors.

TECHNICAL ANNEX

1 S&T EXCELLENCE

1.1 SOUNDNESS OF THE CHALLENGE

1.1.1 DESCRIPTION OF THE STATE-OF-THE-ART

High blood pressure, a global concern

Over the last three decades, the status of high blood pressure (BP) has increased from being the fourth risk factor for global disease burden in 1990 for both females and males, to the first in females and the second in males in 2016 (last Global Disease Burden Study) (1) (2). The increase in annual mortality over this time period has accounted for more than 2 million deaths (1). Therefore, improvement in BP control rates is probably one of the most beneficial steps that can improve not only life expectancy, but also the quality of life for millions of people with immediate and measurable results. Despite the advances in the knowledge of hypertension (HTN) mechanisms, the introduction of new antihypertensive drugs and the large number of campaigns alerting health care providers, stakeholders and populations, there has only been a modest fall in the proportion of the population with high BP (3).

Cardiovascular disease to which HTN is the major contributor has been dubbed, the largest epidemic known to mankind. The number of adults living with HTN worldwide has nearly doubled since 1975, from 594 million to 1.1 billion in 2015, (4) although the global population systolic BP has decreased slightly (-0.8 mmHg per decade in men and -1.0 mmHg in women, from an initial age-standardised mean of 128.1 and 124.4 mmHg, respectively). Trends, however, vary significantly across regions and countries. Systolic BP is currently highest in low-income and middle-income countries. Moreover, the highest levels of BP worldwide have shifted from high-income countries to low and middle-income countries in south Asia and sub-Saharan Africa. Meanwhile, BP has been persistently high in central and Eastern Europe.

Although the decrease seems to have begun before or in the absence of specific interventions for risk factors and scale-up of treatment, and is only partly accounted for by the measured risk factors and treatment. The partly unexplained nature of these favorable trends necessitates speculation about their drivers, which might include unmeasured improvements in early childhood nutrition and year-round availability of fruits and vegetables, which might increase the amount and regularity of their consumption.

It is worth emphasizing that although evolving technology can offer the means to measure complex functions of cardiovascular physiology, the basic phenotype remains BP, and all other measurements are meaningless unless BP is measured accurately. This has been stated in the Lancet Commission on Hypertension: “*In hypertension, blood pressure is an almost ideal biomarker. Blood pressure is causally related to the development of the condition, defines the condition, predicts the outcome, is the target of therapeutic interventions, and serves as a surrogate marker to assess the benefit of therapies. Therefore, the role that other biomarkers could have in hypertension requires careful thought*”.

Knowledge on the status of BP control rates and trends overtime in Europe is relevant due to the huge impact of cardiovascular diseases (CVD), while the most direct diseases are associated with HTN (5). A clear picture of control rates and trends, as well as to establish comparisons among countries is extremely difficult, in part due to the high variability in the methodology applied and even in the thresholds to define BP control. Moreover, even differences between regions within the same country exist. The continuing need to improve the control of high BP has been highlighted in a report from the World Health Organisation (WHO) (6) and a fact sheet issued by the World Hypertension League and the International Society of Hypertension (7).

Despite dramatic medical advances over the last few decades, CVD remains a leading cause of death globally and the number one cause of death in the European Union, accounting for 42%. Lately, it has been possible to relate adult HTN and organ damage to several abnormalities in youth.

The *hypertensive epidemic* has become a serious public health problem worldwide. In 2008, a white paper was published by a group of researchers in HTN with a call for action in order to improve the control rates. The manuscript identified the key challenges in the treatment of HTN and suggested recommendations for improving control (12). Despite some improvements, in 2016 a new publication (5) pointed out the fact that six challenges are still present: inadequate primary prevention, faulty awareness of risk, lack of simplicity in the treatments, therapeutic inertia, insufficient patient empowerment, and unsupportive healthcare systems. Therefore, in order to continue with the advances in BP control, supplementary effort is necessary, since what was achieved in the past reflects a slow improvement. Then, focusing actions on early life, children and adolescents, and assessing the origins of this epidemic is a key issue.

Prevention during childhood and adolescence

High BP is a clearly established, but modifiable, risk factor for early disability and death. Although most of the adverse outcomes occur in adulthood it has become clear that high BP is a life course problem that can become evident in early life. While few would dispute the importance of taking effective steps to identify and manage this condition in middle-aged and older people, relatively little attention has been paid to the problem of high BP in children and adolescents.

The broad present interest in the field of HTN in children and adolescents (9) (10) stems from the desire of health care professionals to offer, and patients to receive, the best possible care. This care should be consistent, efficient and should close the gap between what clinicians do and what scientific evidence supports. However, there is a lack of solid, trial-based evidence for recommendations on diagnosis and management of high BP in children and adolescents.

To fill this gap a commitment should be made to embark on a concerted Action that will provide new important evidence over the next several years. The necessity for a definitive pan-European Action to increase the bulk of knowledge in the prevention, diagnosis and treatment of high BP in children and adolescents is absolute; its absence inhibits consensus across different research domains and detracts efforts to introduce changes in clinical practice. Working for the future, the progress to date should provide an impetus for research advances that may translate into clinical practice. Prevention could assure not only improvement of life expectancy but also better quality of life, and lower costs for public health care systems, keeping people active and healthy.

Improvements in the prevention of blood-pressure-related diseases will be achieved not only by better clinical treatment strategies for people already receiving blood-pressure-lowering therapy, but also through system-based strategies that ensure low blood pressure levels across populations. Despite this knowledge, the largest proportion of funding and research activities is still projected towards individual pharmacological and device-based treatment, such as new antihypertensive drugs, the best combinations of antihypertensive therapy, or new strategies to treat resistant hypertension.

1.1.2 DESCRIPTION OF THE CHALLENGE (MAIN AIM)

Areas of intervention

The scientific and clinical community, as well as the decision-makers, stakeholders and the overall society, must face some critical problems related to the high BP in children and adolescents as a cardiovascular risk factor. In particular, there are some urgent areas of intervention that are summarised below.

Assessment of Hypertension Prevalence in Europe: Since the 1970s, the prevalence of HTN in children has increased ~4-fold (8). It is estimated that the prevalence of HTN in American and European children are the following: specifically 3.5% of US children are hypertensive, 2.2 - 4.9% of central European children and 9 – 13% of Southern and Western European children (9). Prevalence of HTN also increases with age (9). The data are worrying because HTN in childhood is usually already linked with cardiovascular risk factors and intermediate markers of target organ damage (e.g. left ventricular hypertrophy or thickening of the carotid artery vessel wall) (10).

Definition of Hypertension in the Paediatric Population. The definition of HTN in children and adolescents is still based on the normal distribution of BP in healthy children and not on the cardiovascular morbidity and mortality or on the risk to develop early organ damage associated with a certain level of BP. Clinicians can use the available pediatric normative BP data to determine whether BP is within the normal range or is at a level that warrants attention or preventive intervention. Recognition that HTN can be present in otherwise apparently healthy children and that the early increment of BP tracks into adult life raised the interest and the necessity to include BP measurements in the regular health care of children and adolescents. Two new guidelines have been published over the past three years [6,7]. Both agree on a number of issues but differ on several aspects that impact to a non-marginal degree on clinical practice, i.e. the BP threshold that defines HTN, the classification of the BP categories, and as, a consequence, the therapeutic BP targets. The discrepancies and changes in the BP goals provided by guidelines contribute to uncertainty among physicians.

Accurate measurement and early identification. Despite the advances and the extensive literature on BP in children and adolescents, the solutions to relevant questions are still pending. The accurate measurement of BP is a prerequisite in adults and in children for the reliable diagnosis of HTN and the avoidance of misdiagnosis and over-or under-treatment. There is strong evidence that early identification of high BP and early intervention result in successful management, which has an important impact on long-term outcomes of adulthood cardiovascular health (11). So, the development of precise BP measurement protocols, assessment of HTN and therapeutic interventions within the paediatric population are vitally important to prevent that the children of today will become hypertensive adults in the future.

Out of office BP measurements. The main methods for noninvasive measurement of BP are the auscultatory method using conventional mercury or aneroid devices and the automated method using electronic, mostly, oscillometric devices. Although automated electronic devices are currently recommended and widely used for 24-h Ambulatory BP monitoring (ABPM), home and office BP measurements, the published evidence on their accuracy in children and adolescents is limited. Introduction of methods to assess BP values (24-h ABPM and home BP) that claim to be better than the classic BP office measurement has given a new dimension to the problem. Despite having been introduced in clinical practice, no evidence about the validity of these techniques is available. The provision of comparative data and insights about the effectiveness of using any new technique is mandatory, also with respect to the high prevalence of HTN-induced organ damage. It is worth emphasizing that although evolving technology can offer the means to measure complex functions of cardiovascular physiology, the basic phenotype remains BP, and all other measurements are incomplete unless BP is measured accurately (23)

Validation of BP Devices for Infants and Children. Accurate measurement is a key element for the evaluation of many medical conditions and for the reliable diagnosis and efficient treatment of HTN. In the last 3 decades prestigious organizations, such as the US Association for the Advancement of Medical Instrumentation (AAMI), the British Hypertension Society, the European Society of Hypertension (ESH) Working Group on BP Monitoring, and the International Organization for Standardization (ISO), have developed protocols for clinical validation of BP measuring devices. All these initiatives aim to standardise validation procedures and establish minimum accuracy standards for BP monitors. Recently, the AAMI, ESH, and ISO experts agreed to develop a single universally acceptable standard (AAMI/ESH/ISO), which will replace all previous protocols (19) (20). This major international initiative is only focused on adulthood and older age, but serves as a good example to accomplish the objectives of this proposal for COST Action.

Assessment of Hypertension-mediated Organ Damage and Development of Screening Procedures: Besides BP values, better knowledge about the natural history of early organ damage is necessary. The assessment of organ damage needs to be optimized, looking for early markers. High BP induced organ damage can evolve concurrently in heart, carotid artery wall, the kidneys, and in the eye vessels, however, the most common approach is to study damage in one or two areas only. Although guidelines agree that assessment of organ damage is required as part of clinical assessment in the presence of HTN, the current evidence only supports albuminuria and assessment of left ventricular hypertrophy. Better knowledge of all of these may contribute to optimize interventions, reducing organ damage and improving long-term prognosis.

Prevention Strategies. The interventions to decrease the worldwide prevalence of HTN are not effective enough, as recent reports have shown (21) (23). Therefore, it may be necessary to reformulate the objectives and to use a different methodology focused on complementary efforts in a different target population with great physiological plasticity, such as children and adolescents. Therefore, a multidisciplinary network of professionals with different points of view and capabilities, may contribute to take a step forward in solving the serious health problem of HTN targeting at its origins or before sustained damage evolves. However, it is important to realise that successful prevention not necessarily avoid events, but usually delays them until a later time. Furthermore, the relevance of perinatal programming opens up new ways to understand the early-life origins of diseases such as high BP. Understanding the interactions among genetics, fetal, environmental, psychosocial and psychological factors in the development of high BP is critical.

THE CHALLENGE (MAIN AIM)

The COST Action **HyperChildNET (Network for blood pressure research in children and adolescents)** is aimed at establishing a European sustainable and multidisciplinary network of internationally renowned researchers, clinicians, early career investigators, health economists, decision-makers, patients, regulatory bodies, nutrition & pharma companies and medical devices manufacturers focusing on acquiring a holistic understanding of the factors affecting high BP in children in order to propose and implement corrective and preventive actions both globally and locally.

All members of the network and the research projects running locally will collaborate by creating Working Groups to coordinate research actions, exchange scientific and clinical knowledge, research findings and best practices. In order to promote the research objectives foreseen, HyperChildNET will organise conferences,

seminars, Short-Term Scientific Missions, Training Schools and will produce reports, studies, guides, strategy documents and action plans to make progress in contributing to solve the challenge.

Figure 1 represents the multi-variable Action and interdisciplinary collaboration in HyperChildNET.

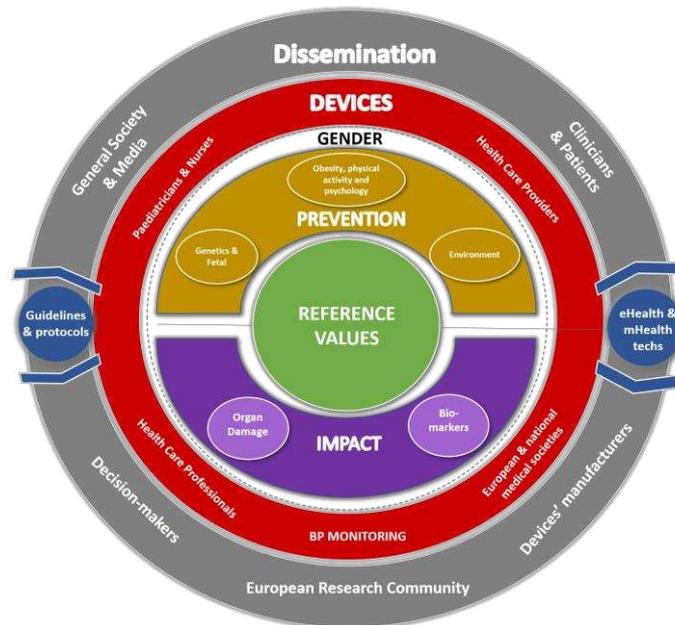


Figure 1. Visual summary of multi-variable interaction in HyperChildNET networking

1.2 PROGRESS BEYOND THE STATE-OF-THE-ART

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

To date hypertension is responsible for 7.1 million deaths per year worldwide, and is closely related to other cardiovascular diseases (CVD) such as ischemic heart disease and stroke. CVD linked to high BP is the primary cause of mortality in Europe generating yearly costs of approximately 1 billion euros per year (18). During the last decade several public health policies have tried to decrease the incidence and prevalence of HTN. However, these well-intentioned public policy initiatives have achieved little success (13). Due to the high prevalence of HTN, 45% of the general population and 30-45% of the European population (14) (15), encouraged by the WHO and National and International Public Health Systems, the European Commission has invested in HTN research.

Although long considered a disease of aging, its prevalence is increasing in children and adolescents (16) (17). Importantly, the negative and potentially severe consequences of high BP are not limited to adulthood. Evidence of target organ damage, such as left ventricular hypertrophy and pathological vascular changes have been found even in young children and already in children with newly diagnosed high BP. Even subtle neurological changes, which manifest as reduced cognitive function, have also been detected among children with high BP. Without intervention, high BP in childhood will increase the risk of premature CVD consequently effective preventive interventions that are applied early in life will modify disease progression. (10), (11), (12)

Despite the body of emerging evidence, paediatric HTN has received less recognition than diseases with fewer potential consequences. The increasing prevalence of high BP in children and adolescents worldwide needs to be evaluated in terms of health care burden and economic impact (24) (25). Given that children with high BP are likely to become adults with high BP, with all the attendant HTN-related sequelae, the impact will be substantial. Alternatively, if appropriate attention is applied to identification, evaluation, and management of children with high BP the long-term benefit will also be substantial.

It is clear that paediatric high BP will further contribute to the current epidemic of CVD unless it is given the attention it deserves by policy makers, health care providers, schools, parents, caregivers, and society as a whole. Action is required to address this problem in one of the most vulnerable and precious sectors of our society: the children who should be able to rely on us to provide the care they deserve.

The EU has funded the on-going ENS@T-HT project in the Horizon 2020 Research and Innovation project into HTN and personalised treatments (European Union's Horizon 2020 research and innovation programme under grant agreement No 633983). There are two main aims of the ENS@T-HT: i) to investigate the specific types of HTN and ii) to define, if possible, specific profiles based on system biology "-omics" approaches to

define individualised treatment. Also, the REALTA project funded by the H2020-EU.1.1.-EXCELLENT SCIENCE- European Research Council (ERC) (Project ID: 754308) aims to improve the treatment of HTN through a novel medical device development using the implementation of the ablation technology. In addition to these on-going projects, recently (18/04/2018) a new call (Better health and care, economic growth and sustainable health systems, H2020-SC1-BHC-2018-2020), included the topic: Global Alliance for Chronic Diseases (GACD) - Scaling-up of evidence-based health interventions at population level for the prevention and management of HTN and/or diabetes.

Regarding COST, two funded Actions have been identified in relation to HyperChildNET. 'Realising the therapeutic potential of novel cardioprotective therapies' (CA16225), highlights the importance of preserving cardiac function and preventing heart failure by using novel cardioprotective therapies. The 'Network for Research in Vascular Ageing' (CA18216), aims to refine, harmonise and promote the use of vascular ageing measures to improve clinical practice and to reduce the burden of CVD globally. However, non of these COST Actions target a profound research about the connection of paediatric age with adulthood and old age.

In any case, collaborating with both Actions will provide an added value for HyperChildNET, so specific tasks will be foreseen to promote networking with these Actions, which will result in mutual benefits.

In sum, currently there are no H2020 projects, H2020 calls, or COST Actions especially focused on paediatric high BP, despite the fact that improving the early identification and management of HTN in childhood could significantly decrease the incidence and prevalence of HTN in adulthood.

Progress beyond the state-of-the-art

The First Report on BP control in children was published in 1977 and has been updated on a regular basis. However, even in the latest versions of BP guidelines (16) (17), there are still crucial discrepancies, lack of consensus and knowledge gaps in relevant areas:

- Many BP measurement devices are not effectively validated for children and adolescents
- Lack of knowledge on key biomarkers involved in BP.
- There are no uniform data on reference values for office and 24-hour ABPM in this population.
- Absence of global unified criteria on HTN diagnosis.
- Lack of knowledge on the accurate relationships with other factors, in the risk to develop high BP, such as:
 - Gender
 - Nutrition and Obesity
 - Physical activity
 - Psychological factors and behaviour
 - Environment and lifestyle
 - The interaction between biological and relevant environmental factors
- The proper assessment of early organ damage on cardiac, vascular and renal structures.
- The role of eHealth and mHealth to improve diagnosis, monitoring and prevention.
- Strategies to design more effective protocols, guidelines and policies.
- Lack of adequate spread of knowledge at different levels; from family, school, social groups and the society.

By collaborating to answer persistent questions and striving to achieve consensus, the global community will get much closer to decreasing the CVD burden acting in our most vulnerable population.

The most active European initiative in this field is the "Working Group on Hypertension in Children and Adolescents" hosted by the European Society of Hypertension. HyperChildNET will go beyond this Working Group by:

- Providing a multidisciplinary and multi-actor approach since it involves industry, stakeholders, target (patient) groups, researchers and clinicians in the networking activities.
- Widening its scope with more ambitious goals taking into consideration a holistic approach of all the variables involved in blood pressure regulation in children and adolescents.
- Generating many networking activities not addressed by the ESH Working Group, such as Short-Term Scientific Missions, Training Schools, regular open seminars and global dissemination actions.
- Enlarging the community through the involvement in HyperChildNET of world-leading researchers together with Early Career Investigators across Europe and other international partners.

1.2.2 OBJECTIVES

1.2.2.1 Research Coordination Objectives

The COST Action is a multidisciplinary network with participants from Europe, focusing on the urgent topic that is high BP. The COST Action will promote coordinated and collaborative activities on personalised preventive

measures for children and adolescents across Europe. The aims are to exchange and disseminate specific knowledge about factors that will improve the prevention of BP elevation. This will be achieved by focusing on the on-going and future actions around the following objectives:

- **RCO1.** To benchmark, assess and select suitable devices for office BP monitoring in children and adolescents that fulfil the overall criteria of the universally acceptable standard (AAMI/ESH/ISO).
- **RCO2.** To define reference values for BP that can be applied all over Europe. This will be cornerstone for the definition of uniform criteria that allow a better stratification and follow-up of HTN in children. This is also the starting point for a better definition of BP categories.
- **RCO3.** To define the best methodological approach for the European clinical and research community to assess hypertension-induced organ damage.
- **RCO4.** To produce guides, publications and ICT-based tools to prevent high BP in children and adolescents taking into account different confounding factors (obesity, physical activity, eating patterns, smoking, social and psychological factors, family communication skills) for a wide range of target groups (clinicians, researchers, decision-makers, patient organisations, families, media and general society representing organisations).
- **RCO5.** To assess the economic impact of recommended policies and stakeholders' intervention.

1.2.2.2 Capacity-building Objectives

This COST Action incorporates a strong multidisciplinary network that, through the Activities and Deliverables described below, will carry out the agenda specified in the Coordination Objectives. In doing so, the Action will complete the following Capacity-Building Objectives:

- **CBO1.** To promote Workshops, Conferences, Short Term Scientific Missions (STSMs) and Training Schools (HyperChildNET Academy), for knowledge-exchange focusing on a topic of clear scientific and socio-economic application through joint actions.
- **CBO2.** To enable the sharing of best clinical practice and scientific state-of-the-art within a European context, which will also sustainably improve collaboration. This will be achieved through Training Schools (HyperChildNET Academy) and capacity building for Early Career Investigators (ECIs).
- **CBO3.** To adopt an interdisciplinary approach to the research agenda by involving medical practitioners, nurses, policy makers, medical device OEM and scientists in the Action, as required for successful adoption of best practices and cross-national cooperation. The HyperChildNET Ecosystem of Stakeholders locally and trinationally (a global network of stakeholders) will be created from where expertise on national actions can be accessed by all interested parties in European countries.
- **CBO4.** To promote the sustainability of the network beyond the life of the Action by encouraging network members to develop collaborative funding applications, continuing the liaison established among researchers after the duration of the Action and maintaining the website as a sustained open resource for researchers, clinicians and policy makers.
- **CBO5:** To foster international cooperation between researchers from COST member countries, COST Near Neighbour Countries (NNC) and International Partner countries (IPC), bringing together different disciplines to enable breakthrough scientific developments in this field of research.
- **CBO6.** To increase the overall awareness of the importance of high BP along childhood, and how to halt the growing epidemic of related factors.

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

The European and the US Guidelines are the great references for the management of high BP in children. Although both guidelines have similarities, there are many differences that have to be solved (16) (17) (8). Among others:

- i) the underlying definition and threshold for HTN,
- ii) the screening protocol for early diagnosis and prevention,
- iii) assessment of organ damage

- iv) characterisation and identification of medical devices especially validated for children and adolescents and
- v) recommendations for out of office BP, for the diagnosis and management of high BP.

HyperChildNET foresees concrete and achievable objectives and work plans to take a significant step in the global challenge of overcoming the discrepancies between these Guidelines. In fact, the core of HyperChildNET is formed by a group of researchers who has been working together for more than 15 years. All of them are relevant members of the most representative European clinical and research structures, so this COST Action will not replicate any previous work but will contribute pioneering research going beyond the state of the art and facing the most critical challenges affecting high BP in children and adolescents.

The starting point of the challenge is to build-up a real multidisciplinary, well-functioning network that will be able to increase knowledge in order to improve the diagnosis, management and follow-up of high BP in children; consequently, improving their health and their quality of life, decreasing the incidence and prevalence of adulthood HTN. To obtain these objectives, the most important innovation will be the methodology used. All professionals involved in HyperChildNET will use an innovative, prospective approach instead of the retrospective evaluation usually done for the preparation of guidelines.

For the first time, in HyperChildNET a large scale and long-term network of researchers will coordinate and monitor their on-going research actions on high BP in children and adolescents to perform jointly designed research, whose homogeneous and comparable results will result in publication of joint protocols, guides, publications and policy proposals.

2.2 ADDED VALUE OF NETWORKING IN IMPACT

2.2.1 SECURING THE CRITICAL MASS AND EXPERTISE

The present situation of BP among the younger population needs a network in order to improve the diagnosis, management and follow-up. High BP in children and adolescents is related to a wide range of variables, internal and environmental, modifiable and non-modifiable, genetics and acquired, which requires a multidisciplinary perspective that can be provided by a solid network of the best professionals in each field and avant-garde approaches by Early Career Investigators.

In HyperChildNET world-leading researchers, early career investigators and industry representatives collaborate, providing relevant skills, solid background and work experience in the area of high BP in children and adolescents, that will be essential for achieving the Action objectives. In addition, HyperChildNET will mobilise key stakeholders of the society such as policy makers, parent associations, schools, CVD patient's associations, etc. Leading organisations at a national and international level will participate in the Action, where they will describe and compare their best practices.

The network builders and their research groups encompass expertise in all necessary aspects to fulfil defined tasks and to reach stated aims. During the lifetime of the Action, gaps in the network will be monitored continuously in WGs reporting to Management Committee (MC). Paediatric researchers and research groups in COST member countries have performed internationally acknowledged, distinguished research, thus, the present Action will build on experience from previous research in the area of high BP of children and adolescents as the most effective mechanism to prevent future cardiovascular risks. This will allow increasing the efficiency of the network and avoiding any duplication with previous or on-going research.

The Action brings researchers from nationally funded research and international partners together. HyperChildNET encourages gender, geographical and age balance; both Early Career Investigators and senior researchers will be encouraged to participate in the networking activities from COST countries, ITC and Non-COST countries.

The establishment of new contacts is expected during the lifetime of the project in order to increase the COST network. Interactions and scientific knowledge exchanges during workshops, seminars and Training Schools (HyperChildNET Academy) will facilitate new collaborative networks and research axis. As a consequence of the developed outputs, new excellent projects will be developed to complement and advance in the prevention of CVD during lifetime through preventive measures for children and adolescents.

The network of Proposers is formed by experts bringing together the required competences and perspectives needed for the successful implementation of the WGs to reach the expected goals. Among them, there is a significant number of research experts, clinicians, epidemiologist, from Academy, Scientific Societies, Health Care Systems decision makers as well as stakeholders from the industry and associations representing citizens. In addition, the experts involved in HyperChildNET are, in most cases, active members of relevant networking initiatives concerning European Guidelines and Working Group on Hypertension in Children and Adolescents. These members will contribute to leverage existing efforts within the framework of the COST Action.

2.2.2 INVOLVEMENT OF STAKEHOLDERS

The following table describes the key stakeholders, their current and future involvement and the benefits for them derived from the implementation of the COST Action:

KEY STAKEHOLDERS	INVOLVEMENT	ADDED VALUE FOR THE STAKEHOLDERS
Basic and clinical researchers	Already participating in the Proposers' network and Working Groups. More researchers will be invited to participate prioritising COST Inclusiveness Countries. Gender issues will be taking into account as well as a special interest in Early Career Investigators.	Joint coordination and mutual enrichment of local ongoing research projects. Generation of new joint research projects. Harmonised and concerted methodology for future clinical studies. Global agreement in the area of BP devices, reference values, impact and prevention of high blood pressure in children and adolescents.
Paediatric clinicians and health care professionals	Already participating in the Proposers' network and Working Groups. More professionals, experts and decision-makers will be invited to participate prioritising COST Inclusiveness Countries.	Internationally validated knowledge and guidelines for BP devices, reference values, patient categorisation, improved diagnosis and treatment.
Health care decision-makers		Knowledge and guidelines to improve BP prevention from the paediatric age to provide more effective treatments and reduce future budget burden in adulthood.
Industry: Devices, Nutrition, Pharma		Technical knowledge for devices' manufacturing and setting, as well as for the development of new products within the nutrition and pharma sectors.
Patients and families	Already participating in the Proposers' network and Working Groups. More networks will be included representing the associations of patients and families both at national and international level.	Improved diagnostic, treatments and prevention measures to reduce high blood pressure. Better access to scientific evidence-based information that has been validated and harmonised by the international scientific and clinical community.
Media	Not to be included directly. These organisations will not become formal members of the network but are also considered relevant stakeholders.	Valuable content to increase awareness on the impact of High Blood Pressure in children and adolescents as well as to promote prevention measures.

PLAN FOR INVOLVING THE MOST RELEVANT STAKEHOLDERS

Beyond the current network of Proposers, HyperChildNET will involve further professionals from key stakeholders in COST countries and COST Inclusiveness Countries by implementing the following actions:

- The Action is promoted by key international societies and European networks which presently include key stakeholders both at national and international levels. Therefore, as a “snow-ball effect”, the partnership has the capacity to progressively increase the network by involving other professionals from the target stakeholders.
- HyperChildNET Ecosystem of Stakeholders. Creating national networks to disseminate information, outputs and findings of the Action. These organisations and professionals will be invited to join seminars, workshops, conferences and related activities.
- Other organisations will be involved in the network in order to connect all the parties related to this field: parent associations, school's networks, public bodies, social researchers, medical charters, patient associations, industrial companies, etc.
- HyperChildNET will also sign collaboration agreements with other networks in Europe and Worldwide, in order to jointly develop actions with a synergetic potential (e.g. projects and networks with different goals but also targeting the young population and professionals working with children and adolescents).

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

HyperChildNET includes as secondary proposer a world leader in the design, manufacture, and marketing of a broad portfolio of high performance analog, mixed-signal, and digital signal processing (DSP) integrated circuits (ICs), in concrete, this proposer is a manufacturer of Multi Parameter Bedside and Diagnostic Monitors (including blood pressure devices). The corporate headquarters of this company are located in the USA. The participation of researchers representing this company is crucial in the Work Group 1, Blood Pressure Devices, in order to provide key knowledge from the industry; in the same way, industry researchers will obtain fundamental feedback from the COST network to adapt future Multi Parameter Bedside and Diagnostic Monitor Devices for blood pressure to the specific requirements of patients at paediatric age. Another world leader

manufacture of blood pressure devices is member of this COST Action. The researchers representing this company come from the European Headquarters in The Netherlands, but in close collaboration with the global headquarters of this multinational located in Japan.

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 Action is implemented through concerted activities, with research being carried out and financed by the participating countries, while HyperChildNET will provide coordination and integration through networking activities. Therefore, the Action will focus on providing the means to discuss, refine, plan and share on-going findings and results, while studies and trials will be performed by the scientists and clinicians as part of their local research projects.

HyperChildNET is expected to have an impact on scientific/medical, technological and socioeconomic domains.

- Scientific/medical domain: Synergistic actions at various levels (professional societies and international expert committees, general practitioners, pediatricians, nurses and other healthcare providers, industry, decision-makers, schools, parents, media and general society) should be successfully implemented in order to limit and reduce the HTN in children and adolescents. In concrete, the following impacts are foreseen:
 - Increased accuracy of the HTN diagnosis in paediatric patients by the clinicians and health care providers. This will be achieved by the needed global agreement on the BP reference values and the consensus of the different categories and ranges (how to measure, when, how many times, what equipments to be used, what values are normal, different groups and subgroups of patients)
 - Accurate assessment of target organ damage and the effects in the paediatric patients as future adults on risk of cardiovascular diseases.
 - Effective treatment and prevention (corrective measures, pharmacology, number of follow-up visits, how to reduce the risk and the implementation of crucial prevention actions)
 - Reduce global uncertainty and, therefore, increase certainty among researchers in the area of BP applied to children and adolescents.
 - Implementation of policy roadmaps by decision-makers in health ministries, regions and hospitals in Europe and worldwide taking into account the guidelines and recommendations of the global network promoting HyperChildNET.
 - Increase awareness of the families, patients, media and the general society about the need to implement prevention measures in order to reduce target organ damage in paediatric patients as well as cardiovascular diseases in the adulthood.
- Technological domain: Adaptation of the BP monitoring devices by the industry according to the instructions generated by the global network. Improvement in the knowledge for the design and development of new devices for clinical BP measurement, as well as the use of *eHealth/mHealth* for prevention, diagnosis, management and follow-up of high BP.
- Socioeconomic domains: Reduce the economic burden in the health care systems by implementing the most effective treatment in childhood as a preventing measure to reduce costs of cardiovascular related chronic diseases in adulthood. Assess the economic impact on national healthcare systems depending on reference values (childhood Vs. adulthood). Budget reduction and efficiency with an improved and fast diagnosis of BP and with more effective treatment methods for children and adolescents. Highly qualified jobs are also expected to be created.

3.2 MEASURES TO MAXIMISE IMPACT

3.2.1 KNOWLEDGE CREATION, TRANSFER OF KNOWLEDGE AND CAREER DEVELOPMENT

HyperChildNET's objectives and work plan are mainly addressed to generate and transfer knowledge among professionals representing the stakeholders from a great variety of countries. This network is led by top global researchers in this field who will guide all the participants throughout the process of generating scientific publications, guidelines, protocols and roadmaps.

Furthermore, the joint coordination of local research projects will allow achieving comparable and complementary results and avoiding unnecessary duplications, therefore it will also increase technical and financial efficiency of the related local research projects.

Transfer of knowledge is critical for the impact of the project; thus the network directly involves key stakeholders that will use the created knowledge to:

- Develop and adapt BP devices and their settings to the specific needs of paediatric patients.
- Improve diagnosis, monitoring and treatment.
- Implement policy strategies to encourage prevention and costs reduction in the health care systems: moving from treatment to prevention.
- Increase awareness of the families, educators, children and adolescents, media and general society as a whole.

This knowledge generation and transfer will also be a breeding ground for the ideation of new research projects to be implemented locally or at transnational level with private and/or public funds such as EU Programmes (Horizon Europe, EC Health Programme, EUREKA, Interreg, Erasmus+, etc)

Finally, HyperChildNET also foresees training activities to capacitate Early Career Investigators in order to build and assure the future research community formed by young researchers focused on this specific field of BP in children and adolescents. The online and offline training activities foreseen will provide students core knowledge and critical appraisal skills on this specific topic.

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

HyperChildNET intends to influence a broad audience in terms of geographical location in order to reach out to researchers, clinicians, NGOs, policy makers at sector level, national decision makers, private institutions, and the general public in Europe and beyond. Dissemination will be crucial in order to impact on society and to create awareness about the current problems and the need for monitoring and prevention measures at all levels of the medical community and the overall society.

Three main methods will be used for dissemination:

Events & face-to-face dissemination:

- Management Committee (MC) and WG meetings will facilitate communication among Action members.
- The Annual meetings and International conferences will be organised by the MC, WGs, and local Action member Conference hosting organisations to enable Action members to share insights. These conferences will be promoted to international experts, representatives from central health authorities, relevant representation from civil society (e.g. users), training institutions, clinicians and policy makers to facilitate communication between the partners and forge links between research, policy, and action plans.
- Training Schools under the name of HyperChildNET Academy and organised by the MC, together with local Training Schools hosted by different Action member institutions will be offered in order to strengthen the capacity building of health professionals working with children and adolescents. This initiative will combine presentational and virtual activities in order to allow live interaction but also facilitate access to any interested party.
- Short Term Scientific Missions (STSMs) organised by the MC and local hosts in different Action member countries will facilitate the mobility of ECIs and offer them an opportunity to interact with more experienced researchers.
- Local workshops will be set up by WG members to connect the goals and activities of the Action with local stakeholders.
- Active participation in conferences and events of European and international societies and associations.

Publications, which will be disseminated on the HyperChildNET website, through Facebook, Twitter, electronic newsletters, magazines and in open access journals:

- Scientific reports; meta-analyses and systematic reviews
- Policy reports and executive summaries
- WG reports
- Research guidelines
- Guides and White Book
- Submit a policy brief to the European Parliament's Committee on Environment, Public Health and Food Safety (ENVI).

IT based communication:

- Working Group 5 is responsible for the setting up and maintenance of the website hosted at www.hyperchildnet.eu, and running social media as well as initiating and coordinating media contact. The

website will be a major source of communication and dissemination of information both among Action members and the public outside the Action. The website will provide all the outputs and activities of this Action and these will be publicly available. WGs will produce state-of-the-art papers, summaries, and recommendations on assessment tools and study designs, which will be communicated through the website. It will also include a web-based platform with a repository of best practices on e-Health, especially m-Health, for the prevention of high BP in children and adolescents.

- All the conferences and events will be recorded and uploaded in a 'youtube' dedicated channel to be globally accessible, together with interviews and other videos with relevant content for the stakeholders.
- Along with other social media, the website will be used to invite potential stakeholders to take part in WGs, local workshops, stakeholder conferences, international meetings and Training Schools. Password protection will be used to protect work in progress using a 'Basecamp' project management tool.
- An open and free training module (MOOC based training activity) will be developed and inserted in the website in order to make clinicians and main stakeholders aware of effective prevention measures.
- Media communication and public announcements will be made by Action members in order to increase public attention and debate. Social media including Facebook, blogs, Twitter and LinkedIn will be used to maximise debate and dissemination of knowledge and results. WG5 will have an important role in coordinating media contact.
- E-mail, E-groups, video- and tele-conferencing, and Skype will be used to enable regular on-going communication between Action members.

4 IMPLEMENTATION

4.1 COHERENCE AND EFFECTIVENESS OF THE WORK PLAN

4.1.1 DESCRIPTION OF WORKING GROUPS, TASKS AND ACTIVITIES

The desire to truly focus from different point of views on the urgent topic of high BP in children and adolescents is evident in the structure of the Work Plan.

Five WGs will be created as shown in figure 3. Colours are related to figure 1 representing the variables under the same Working Group.

The rationale for establishing WGs is the research collaboration between nationally funded research groups & projects, as well as to perform systematic reviews, meta-analyses economic evaluations and guidelines. This exchange will enable coordination of European efforts to reveal the interaction effects between different working groups and research goals.

Working Groups will allow exchanging knowledge and expertise within a specific core topic (BP measurement devices, reference values and epidemiology, origins, impact, prevention and finally dissemination) from a multidisciplinary approach. In order for the WGs to best achieve their aims, they will include multidisciplinary research groups, clinicians, health economists, training institutions, nutrition & pharma companies, medical devices OEMs and representatives from all the target groups.

WG1-WG3 are closely related and will perform coordinated research actions and collaborative literature reviews, while WG4 will integrate all the generated knowledge and develop convenient prevention guidelines. The WG5 will involve all partners in disseminating the COST Action as well as its results.



Figure 3. HyperChildNET Working Groups

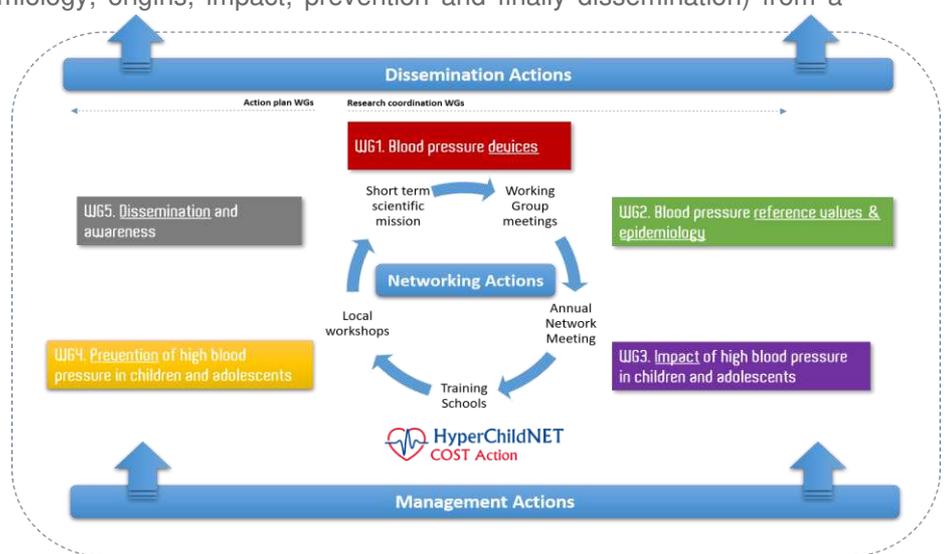


Figure 4. Pert Chart

Finally, the whole Action will be managed by the Management Committee (MC). Each WG will be appointed a Leader, who, in collaboration with the MC, will be in charge of a plan of action for each WG, detailing plans, tasks and methods for execution of their part of the Action, including the planning and follow-up of the allocated Action budget. Each Grant Period the MC will prepare a Work and Budget Plan for the Action.

WORKING GROUPS DETAILS

WG1. BP measurement DEVICES

Objective:

- **RCO1.** To benchmark, assess and select suitable devices for office BP monitoring in children and adolescents that fulfil the overall criteria of the universally acceptable standard (AAMI/ESH/ISO).

Tasks:

- T1.1. Define the criteria to benchmark the different BP measurement devices according to the different BP measurements and BP methods.
- T1.2. Analyse the criteria for validation and the clinical issues affecting the validation procedure.
- T1.3. Generate a map of equivalences among most used BP measurement devices available on the market.
- T1.4. Evaluate new device proposals in order to find out its potential in non-intrusive, non-stigmatizing BP measurement platforms.
- T1.5. Analyse and agree on the new developments to fill the present gaps among clinical practitioners and decision-makers as well as the industrial partners.

WG2. BP REFERENCE VALUES AND DEFINITION OF BP CATEGORIES

Objective:

- **RCO2.** To define reference values for BP that can be applied all over Europe. This will be cornerstone for the definition of uniform criteria that allow a better stratification and follow-up of HTN in children. This is also the starting point for a better definition of BP categories.

Tasks:

- T2.1. Meta-analysis of reports in the most relevant bibliographic repertoires on available data for BP.
- T2.2. Analysis of usable Electronic Health Recordings and data bases of BP values.
- T2.3. Develop reference values using tables with European data based on age, sex and height percentiles. An approach to simplify the criteria for diagnosis of BP categories.
- T2.4. Set the methodology to harmonise future clinical studies in Europe which prospective analysis can validate and enrich reference values established by HyperChildNET.
- T2.5. Carry out an analysis on health care burden of actual high BP in children and adolescents in Europe, and a cost-effectiveness analysis of a population-based versus opportunistic screening of BP with the new defined reference values and thresholds for clinical treatment and follow-up.

WG3. IMPACT of high BP on target organ damage in children and adolescents

Objective:

- **RCO3.** To define the best methodological approach for the European clinical and research community to assess hypertension-induced organ damage.

Tasks:

- T3.1. Meta-analysis of studies assessing hypertension-induced organ damage in children and adolescents and studies in which organ damage has been confronted with organ damage at different organs.
- T3.2. Define methods to assess hypertension-induced organ damage, cardiac and renal parameters in terms of sensitivity, reproducibility, predictive value, cost and potential prognostic value.
- T3.3. Set up a methodology to coordinate and harmonise on-going and future clinical studies to collect valuable and comparable data on target organ damage on children and adolescents.
- T3.4. Elaborate a guide for healthcare professionals about when it is necessary to assess the presence of target organ damage, how and when to repeat during the follow-up.

WG4. PREVENTION of high BP in children and adolescents

Objectives:

- **RCO4.** To produce guides, publications and ICT-based tools to prevent high BP in children and adolescents taking into account different confounding factors (obesity, physical activity, eating patterns, smoking, social and psychological factors, family communication skills) for a wide range of target groups (clinicians, researchers, decision-makers, patient organisations, families, media and general society representing organisations).
- **RCO5.** To assess the economic impact of recommended policies and stakeholders' intervention.

Tasks:

- T4.1. Develop and propose actions in professional daily environments to prevent BP elevation mainly addressed to health care professionals and decision makers.

T4.2. Generate policy action recommendations to provide a better response to this problem assessing the economy impact of each measure (efficiency and effectiveness in childhood interventions and the corresponding health impact and cost reduction in future adulthood)

T4.3. Elaborate and propose prevention actions and recommendations for the parents, patients and educators.

T4.4. Review good and best practices regarding high BP prevention strategies employing e-Health and m-Health services for the developmental age.

T4.5. Design a MOOC e-learning module for both clinicians and main stakeholders (industry, parents, educators, children & adolescents and policy makers) on the most effective measures to prevent high BP among children and adolescents.

T4.6. Create the HyperChildNET Ecosystem of Stakeholders both locally and transnationally and undergo co-creation activities with real representatives of each category in order to understand their specific needs, preferences and behaviours on which later developing suitable prevention strategies and related tools (focus groups / brainstorming sessions / interviews / role playing / shadowing)

T4.7. To perform an economic evaluation of the recommended policies and stakeholders' intervention with societal perspective and long term time horizon based on the modelling of the natural history of the disease and the expected effectiveness of the recommended policies for measuring, prevent and control high BP in children and adolescents

WG5. DISSEMINATION and awareness

Objectives:

- To disseminate the results of the HyperChildNet among paediatricians, family doctors, nurses, families, scientific societies and other national and international stakeholders.
- To spread all Action's activities and deliverables through the designed website, social media, and open access journals.
- To disseminate knowledge on paediatric HTN also through target groups (children, adolescents, families and care givers) making use of workshops, clinical programs and municipal programs.

Tasks:

T5.1. Identification of the relevant target audiences, global marketing strategy and corporate image of the network.

T5.2. Description and planning of the dissemination actions to be undertaken every year.

T5.3. Carry out tailored dissemination actions using specific tools in order to achieve effective communication for each relevant target audience. Including submitting a policy brief to the European Parliament's Committee on Environment, Public Health and Food Safety (ENVI).

T5.4. Scientific, clinical and socio-economic evidence through dissemination procedures and activities.

T5.5. Set the overall technical requirements to allow the generation of open data to be comparable and publishable by the research and clinical community as well as the decision makers.

T5.6. Produce a publication with guidelines for the media to prevent high BP in children and adolescents.

4.1.2 DESCRIPTION OF DELIVERABLES AND TIMEFRAME

List of deliverables (the timeframe of each delivery is detailed later in the Gantt chart)

WG1. BP measurement DEVICES

D1.1. Benchmark report according to the different BP methods and measurements.

D1.2. Guide for device accuracy and quality criteria for the main specific use in children and adolescents.

WG2. BP REFERENCE VALUES

D2.1. Report of a map of BP values according to BP measurements and epidemiological factors.

D2.2. Build tables of European reference values for office use merging the existing data and for 24-h ABPM

D2.3. Investing in prevention today, means health and savings tomorrow. Report of reduction of health burden and cost-effectiveness of screening for high BP in children and adolescents in Europe with the new thresholds and reference values.

WG3. IMPACT of high BP on target organ damage in children and adolescents

D3.1. Guide for assessing target organ damage in high BP.

D3.2. Guide for health professionals about when, how and what is necessary to assess biomarkers and target organ damage.

WG4. PREVENTION of high BP in children and adolescents

D4.1. White paper on high BP prevention in children and adolescents (including guidelines, protocols and policy proposals).

D4.2. Guide with specific recommendations for the target groups, parents and educators on how to reduce BP values in children and adolescents.

D4.3. Web-based platform with a repository of best practices on e-Health, especially m-Health, for the prevention of high BP in children and adolescents (inserted in the website)

D4.4. Open and free training module (MOOC based training activity) for clinicians and main stakeholders to guarantee awareness of effective prevention measures (inserted in the website)

D4.5. Report on the economic evaluation (cost-effectiveness) of the clinical and population based public health interventions for BP prevention

WG5. DISSEMINATION and awareness

D5.1. Dissemination strategy guidelines for the whole COST Action.

D5.2. Web and new social networks accounts for HyperChildNET.

D5.3. Policy brief to the European Parliament's Committee on Environment, Public Health and Food Safety.

D5.4. List of annual dissemination activities and their audience impact.

4.1.3 RISK ANALYSIS AND CONTINGENCY PLANS

No.	Risk	Probability	Contingency plan
1	Internal: low commitment, availability and productivity	Low	This risk will be minimised and managed by using well-established methodologies for project planning and project control. Each WG leader will be responsible for monitoring the quality of the produced work. Furthermore, an online management tool will allow every participant to know exactly the work in progress and next deadlines.
2	Consensus on crucial topics (terminology, causes, solutions, deliverables) not achieved	Medium	Use of established consensus-finding tools such as the analytic hierarchy process (ahp), the Delphi method and online facilitation tools. Use of qualified facilitators when necessary. Active participation of network members and stakeholders from the very beginning of the design of Working Groups strategy and work plan.
3	Action outcomes lack credibility with target audiences	Low	Ensuring high level of expertise and experience within all WGs, MC and Core Group. Deploying consistent and broad communication strategy throughout the Action's lifetime to ensure strong awareness across all target communities. Ensuring on-going opportunities for key international associations to input and engage with the Action.
4	Connection with decision makers	Low	Strategy created and deployed to engage regulatory and government audiences in the work of the Action in order to ensure recommendation are considered by decision-makers.
5	Milestones and deliverables are not delivered to a high quality	Low	Quality management processes to be used throughout Action, with internal review and scrutiny of draft milestones and deliverables. Recruitment of experienced individuals to the Action.
6	Insufficient current and past research conducted to support Working Groups in their tasks	Low	Wide promotion of COST Action by communication, dissemination and evaluation of WGs, in order to stimulate new research and bring forward all relevant current researchers. Use of scientific meetings, congresses and high profile events as further incentives for new research in COST Action areas.
7	Action is too ambitious in goals, milestones and deliverables	Low	This COST Action is not intended to study and interpret the long-term periods by implementing prospective actions, because many years would be necessary to study transition of patients from childhood to adulthood. On the contrary, the concrete objectives and actions foreseen in HyperChildNET are achievable during the first four-year period since the working methodology is mainly based on meta-analysis, retrospective biostatistic analysis, share & processing databases from stored electronic records (anonymously) and the coordination of current medium-term local research projects. However, the impacts will continue after the first 4 years since there are actions for the sustainability of the network and also because a key result of HyperChildNET is to set the methodology to harmonise future research actions, clinical studies and clinical trials on this topic in Europe, which future prospective analysis will increase the impact of HyperChildNET. Finally, in order to monitor this risk, on-going review of goals, milestones, deliverables will be carried out through regular monitoring reports from each WG (every 3 months).

4.1.4 GANTT DIAGRAM

	YEAR 1				YEAR 2				YEAR 3				YEAR 4			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Management & evaluation																
Kick-off meeting	x															
Monitoring and coordination meetings		x		x		x		x		x		x		x		x
On-line meetings	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Evaluation reports				x				x				x				x
Networking																
Working Group meetings		x		x		x		x		x		x		x		x
Annual Network Meeting				x				x				x				x
HyperChildNET Academy (Training Schools)				x				x				x				x
Local workshops					x				x				x			x
Short-Term Scientific Mission		x				x				x				x		
Dissemination																
1 st COST Conference								x								
2 nd COST Conference																x
Website	x															
Booklet and poster	x															
Social media																
Social networks																
Working groups																
T1.1																
T1.2								D1.1								
T1.3															D1.2	
T1.4																
T1.5																
T2.1				D2.1												
T2.2																
T2.3														D2.2		
T2.4																
T2.5														D2.3		
T3.1																
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T4.4													D4.3			
T4.5														D4.4		
T4.6																
T4.7												4.5				
T5.1	D5.1															
T5.2																
T5.3	D5.2												D5.3			
T5.4																D5.4
T5.5																
T5.6																

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