

HyperChildNET COST Action CA19115: report of the task force

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HyperChildNET COST Action CA19115: report of the task force

E. Lurbe^{a,b}, G. Mancía^c, D. Drozd^d, S. Erdine^e, F. Fernandez-Aranda^{a,f}, M. Litwin^g, M. D. Sinha^h, G. Simonettiⁱ, S. Stabouli^j and E. Wühl^k on behalf of the HyperChildNET Members

^aCIBER Fisiopatología de la Obesidad y Nutrición (CIBEROBN), Instituto de Salud Carlos III, Madrid, Spain; ^bDepartment of Pediatrics, University of Valencia, Valencia, Spain; ^cDepartment of Pediatrics, University of Milano-Bicocca, Milan, Italy; ^dDepartment of Pediatric Nephrology and Hypertension, Jagiellonian University Medical College, Kraków, Poland; ^eUniversity of Istanbul Cerrahpasa School of Medicine, Istanbul, Turkey; ^fDepartment of Clinical Sciences, University Hospital of Bellvitge-IDIBELL, University of Barcelona, Barcelona, Spain; ^gDepartment of Nephrology, Kidney Transplantation and Hypertension, The Children's Memorial Health Institute, Warsaw, Poland; ^hDepartment of Paediatric Nephrology, Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, Kings College London, London, UK; ⁱInstitute of Pediatrics of Southern Switzerland, Ente Ospedaliero Cantonale (EOC), Bellinzona, Switzerland; ^j1st Department of Pediatrics, Aristotle University of Thessaloniki, Hippokratia General Hospital of Thessaloniki, Thessaloniki, Greece; ^kMedical Faculty Heidelberg, Center for Pediatrics and Adolescent Medicine, Division of Pediatric Nephrology, Heidelberg University, Heidelberg, Germany

ABSTRACT

Purpose: Despite dramatic medical advances over the last few decades, cardiovascular disease remains a leading cause of death globally. High BP is 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 however, relatively little attention has been paid to the problem of high BP in children and adolescents.

Materials and methods: Being aware of the problem and the needs, the Task Force of the ESH Guidelines in children and adolescents took the initiative to move forward in the field, identifying the COST Action program. A proposal, HyperChildNET, was submitted, approved and funded for 4 years starting in October 2020.

Results: The aim of the Action has been to establish a European sustainable and multidisciplinary network of researchers, clinicians, early career investigators, health economists, decision-makers, regulatory bodies, and medical devices manufacturers under the umbrella of the European Commission in order to acquire a holistic understanding of those factors affecting high BP in children and adolescents in order to propose and implement preventive and corrective actions. All the activities carried out during the 4 years are described.

Conclusions: HyperChildNET offers a European perspective of the issue giving us the opportunity to develop new strategies and objectives moving forward in the field.

PLAIN LANGUAGE SUMMARY

WHAT IS NEW: The novelty is the development of one network of excellence, HYPERCHILDNET, devoted to a holistic approach to the relevance and importance for health of blood pressure in children and adolescent across Europe. HyperChildNET is a multidisciplinary network of experts from different areas, researchers, clinicians, early career investigators, health economists, decision-makers, regulatory bodies, and medical devices manufacturers under the umbrella of the COST Action Programme of the European Commission.

WHAT IS THE IMPACT: HyperChildNET has become a solid and powerful network that has promoted: a) material for empowering paediatrician and professional's working with children; b) support for young researchers; c) developing tools to facilitate classification of blood pressure categories in children and adolescents; d) networking in cooperation with European Scientific Societies as European Society of Hypertension and the European Academy of Paediatrics enlarging the impact of the task developed across Europe.

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Introduction

Over the last three decades, high blood pressure (BP) or hypertension (HTN) has increased from the earlier position as the fourth risk factor for global disease burden (1990), to the first and second position for

global disease burden (2016) in males and females, respectively [1,2]. The increase in annual mortality over this time period has accounted for more than 2 million deaths [1]. This can be opposed by antihypertensive treatment whose adoption has undisputable

protective effects [3]. Therefore, improvement in high BP control rates is unquestionably one of the most beneficial goals to pursue in order to improve not only life expectancy, but also the quality of life for a huge number of people globally. Regretfully, despite the advances in the knowledge of HTN-related mechanisms, the introduction of new antihypertensive drugs and the large number of campaigns alerting healthcare providers, stakeholders and populations, there has only been a modest fall in the proportion of the population with hypertension control [2].

Despite the striking diagnostic and treatment advances that have occurred over the last few decades, CVD remains a leading cause of death globally in the world as well as in the European Union, in which it accounts for 42% of the overall number of fatal events. Hypertension is an established and modifiable, risk factor for early disability and death and although most of the adverse outcomes occur in adulthood it is now long clear that high BP is a lifelong problem that can become evident at a young or even very young age. While few would dispute the importance of taking effective steps to identify and manage hypertension in middle-aged and elderly people, relatively little attention has been devoted to the problem of high BP in children and adolescents.

The broad present interest on HTN in children and adolescents [3–5] stems from the desire of health care professionals to offer, and patients to receive, the best possible care, that is, a care that is consistent, efficient and closes the gap between what clinicians do and what scientific evidence supports. Unfortunately, this is not entirely achievable in children at adolescents because at those ages there is lack of solid, trial-based, evidence for recommendations on diagnosis and management of high BP.

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 need for a clear pan-European effort to increase the bulk of knowledge on the prevention, diagnosis and treatment of high BP in children and adolescents is absolute; its absence inhibits consensus across different research domains and detracts from efforts to introduce changes in clinical practice. Working for the future, the progress to date should provide and impetus for research advances that may translate into clinical practice. Prevention could assure a longer and better quality of life, and lower costs for public health care systems, keeping people active and healthy for longer.

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 both adults and children to guarantee the reliability of the diagnosis of HTN, avoiding misdiagnosis and over or undertreatment. The best way to non-invasively measure BP in children is to use the auscultatory method *via* conventional mercury or aneroid devices and the automated method *via* 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 measurement, the published evidence on their accuracy in children and adolescents is limited. Although some evidence has been collected these methods to assess BP values (24-h ABPM and home BP) are clinically better than the classic BP office measurement method further comparative data and insights about the relative effectiveness and advantages of using these techniques is mandatory, their confronting being inevitably based on their association with organ damage as well as the predictive ability for organ damage to progress with age and regress with treatment, given that, unlike in adults, research in children cannot rely on the risk of overt diseases and death. Besides BP values, better knowledge about the natural history of early organ damage is necessary. The assessment of hypertension mediated organ damage needs to be optimised, looking for early markers and accurate and reproducible quantification. In children hypertension-induced organ damage can affect concurrently the heart, the carotid artery wall, the CNS, and the kidney, the most common condition being to observe damage in one or two territories. This justifies the assessment of organ damage in different territories simultaneously. Better knowledge and repeated assessment of organ damage may contribute to reduce the involvement of organ damage, optimise interventions and improve long-term prognosis. Furthermore, the relevance of perinatal programming [6] opens up new ways to understand the early-life origins of hypertension as well as other diseases. Understanding the interactions among genetics, foetal, environmental in the development of high BP is of critical importance.

Materials and methods

Instrument: COST Action

Being aware of the problem, the unmet needs and the possible solutions, the Task Force of the ESH Guidelines in children and adolescents [3] took the initiative to move forward in the field. Looking for an instrument that could improve knowledge in the

context of collaborative work, the Task Force reviewed the programmes offered by the European Commission, identifying the COST Action program as a potentially effective option. COST (European CO-operation in Science and Technology) is the longest-running European funding programme supporting cooperation among researchers, engineers and scholars by enabling them to jointly develop their own ideas and new initiatives. Founded in 1971, COST is the oldest and widest European intergovernmental programme for transnational Cooperation in Science and Technology involving 38 COST countries (Europe as a continent not only the EU). The COST Action at the time that the proposal was submitted and approved was involved in 294 running actions, 88% of participating researchers indicating carrier advancements with an average of 30 Cost countries and 37% success rate of spin-off proposals in H2020 per action. HyperChildNET was funded for 4 years starting in October 2020.

Objective

The aim of HYPERCHILDNET project has been to establish a European sustainable and multidisciplinary network of researchers, clinicians, early career investigators, health economists, decision-makers, regulatory bodies, and medical devices manufacturers under the umbrella of the European Commission in order to acquire a holistic understanding of those factors affecting high BP in children and adolescents in order to propose and implement preventive and corrective actions.

The COST Action is a multidisciplinary network with participants from Europe, focusing on the urgent topic of high BP in children and adolescents. The COST Action promotes coordinated and collaborative activities and is establishing applications on personalised preventive measures for children and adolescents across Europe. The aims are to exchange and disseminate specific knowledge about factors that will improve relevant outcomes in HTN, including prevention of BP elevation. This is achieved by focusing the on-going and future actions around the following objectives:

The key elements of HyperChildNET were published in Hypertension in April 2023 [7].

Methodology

The working plan includes the role of 5 WGs: WG 1 focuses on the assessment and selection of suitable devices for office BP monitoring in children and adolescents, using criteria that fulfil universally acceptable

standards by the Association for the Advancement of Medical Instrumentation, the European Society of Hypertension and the International Organisation for Standardisation. WG2 is working on the collection of office BP reference values based on large scale and geographically widespread data. WG 3 specialised on the impact of BP values on the development of hypertension mediated organ damage. WG4 focused on prevention and WG5 on dissemination of evidence and clinical information. Each of the WGs developed its activities organising conferences, seminars, support to the researcher, producing reports, and guidelines. The main actions are summarised in the Figure 1.

Results

Educational activities: training schools, dissemination meetings, scientific conferences, webinars

Two training schools have been organised. One was held in Vilnius in June 2022, and one Summer School was organised in Prague in June 2024. Both places were located in inclusive target countries.

To promote and disseminate the research objectives, HyperChildNET has organised regular conferences (Valencia, Istanbul, Krakow, Thessaloniki, Amsterdam, Bellinzona, Heidelberg). These conferences were led by the WG leaders, and this is reflected by the cities where they took place. The first meeting was organised by the Chair of the Action immediately after the pandemic lockdown in Valencia and the last one by the Vice Chair in Heidelberg. All meetings were held in a hybrid manner with an active participation of members of all WGs.

In cooperation with the European Academy of Paediatrics (EAP), HyperChildNET organised two webinars open to all paediatricians in March 2024. The webinars were free of charge, recorded and now available on the website of HyperChildNET. Under the main topic 'Hypertension in children and adolescents' active and dynamic sessions were attended by paediatricians coming from all over the world.

Training and research support

HyperChildNET has distributed a total of 54 grants with different objectives, design and development:

- Short Term Scientific Missions (STSMs): Short-term scientific missions consisted of exchange visits for researchers within their COST Action. STSMs are great opportunities

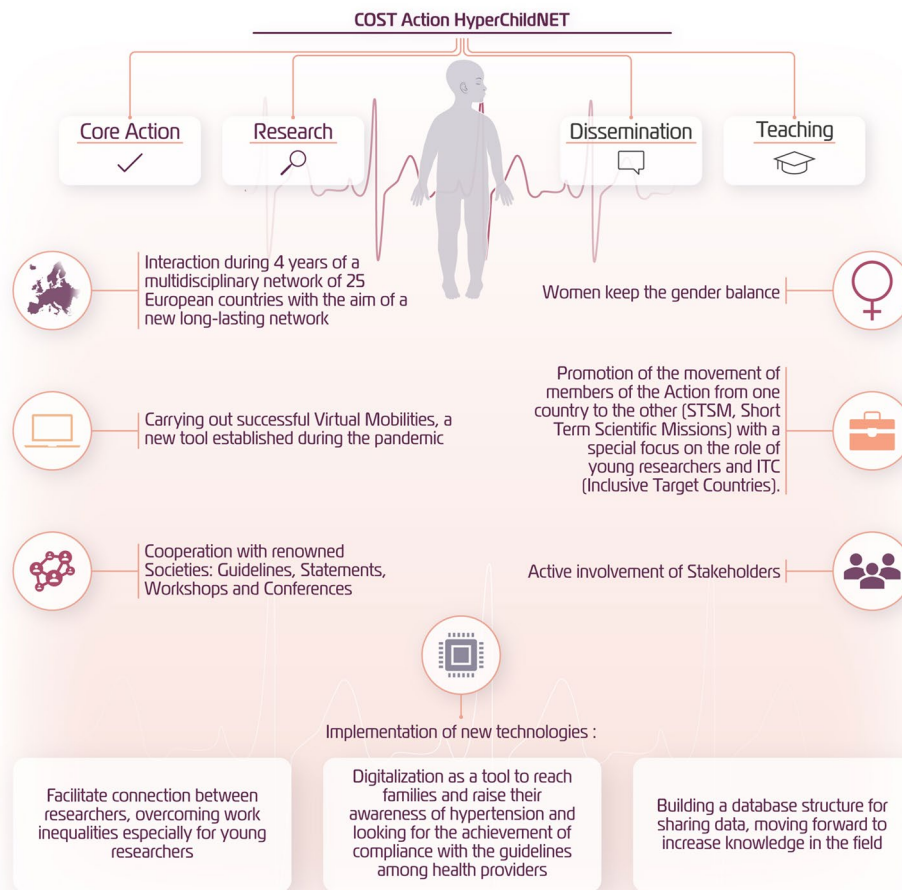


Figure 1. Main actions of HyperChildNET.

Modified from: Lurbe E, Mancia G, Drozd D, Erdine S, Fernandez-Aranda F, Litwin M, Sinha MD, Simonetti G, Stabouli S, Wühl E; HyperChildNET Members. HyperChildNET: A European Network Moving Forward in the Field of Pediatric Hypertension. *Hypertension* 2023 Apr;80(4):e71-e73. doi: 10.1161/HYPERTENSIONAHA.123.20080. Epub 2023 Feb 7. PMID: 36748460.

for researchers to share techniques and gain skills that may not be available at their home institution or laboratory. STSM applicants had to be professionals affiliated to research or innovation organisations (either public or private institutions) in an eligible country participating in the COST Program. The proposal needs to fulfil the eligibility set by COST regarding sending and hosting countries. Overall, 18 grants were awarded with 2/3 to females. Countries receiving and sending applicants were mostly Italy, Spain, Poland and Greece. It is important to mention that some of these STSMs led into publications and presentations at international congresses.

- Virtual Mobilities (VMs): This supported the implementation of research related activities that do not necessarily require in-person presence and were created during the COVID pandemic since at that time movement was

restricted. The success achieved with this kind of grant has led to maintain them within COST Action. Virtual mentoring scheme with special focus on activities and exchanges that can generate capacity and build new skills, particularly for young researchers. Content preparation and coordination of science communication. Overall, 27 grants were awarded with almost equal gender distribution. Similar to STSMs, VMs also contributed to the development of publications.

- Support for attending and participating at scientific meetings:
- ITC Conference grants: ITC conference grants are grants aimed at young researchers and PhD students from ITCs to attend beneficial international conferences that are not organised by COST Actions, in total 5 grants were awarded.
- Dissemination Conference grants: 3 grants were awarded to support the participation of

Action participants to high-level conference to present the work of HyperChildNET.

- Virtual Networking Support (VNS) Grant: One grant aiming at stimulating virtual collaboration among the members of a COST Action was awarded.

It is relevant that the support activities have been prioritised to young researchers and those coming from Inclusive Target Countries (ITC).

Publications

A wide collaboration of members of different WGs of HyperChildNET has produced publications, reports, guides and strategy documents. Scientific papers have been published in peer-reviewed journals (<https://hyperchildnet.eu>), a special issue in *Frontiers in Cardiovascular Medicine* has been led by HyperChildNET, furthermore HyperChildNET has contributed to a special issue in *Nutrients*. A Joint Statement has been published in cooperation with the EAP.

Topics and publications

Devices

- Stabouli S, Chainoglou A, Evripidou K, Simão C, Antza C, Petrou P, Hamdani G, Calpe J, Lurbe E. Comparison of validation protocols for blood pressure measuring devices in children and adolescents. *Front Cardiovasc Med*. 2022 Nov 23;9:1001878. doi: 10.3389/fcvm.2022.1001878. PMID: 36505363; PMCID: PMC9727228.

Ambulatory BP measurements

- Martinez F, Redon J, Aguilar F, Calderon JM, Lurbe E. Persistence and determinants of blood pressure phenotypes according to office and ambulatory blood pressure measurements in youth. *Hypertens Res*. 2023 May;46(5):1257-1266. doi: 10.1038/s41440-022-01159-w. Epub 2023 Jan 13. PMID: 36635525.
- Lurbe E, Redon J, Alvarez J, Grau-Pérez M, Martinez F, Mancia G. Insights From Matched Office and Ambulatory Blood Pressure in Youth: Clinical Relevance. *Hypertension*. 2022;79:1237-1246.
- Álvarez J, Aguilar F, Lurbe E. Blood pressure measurement in children and adolescents: key element in the evaluation of arterial hypertension. *An Pediatr (Engl Ed)*. 2022;96:536.e1-536.e7.

Assessment of hypertension mediated organ damage (HMOD)

- Azukaitis K, Sinha MD, Obrycki Ł, Pac M, Bjelakovic B, Jankauskiene A, et al; HyperChildNET Working Group 3. Disparities between determinants of impaired vascular structure and function in young people with primary hypertension: a systematic review. *J Hypertens*. 2022;40:1369-1379.
- Rus RR, Pac M, Obrycki Ł, Sağsak E, Azukaitis K, Sinha MD, Jankauskiene A, Litwin M; HyperChildNet Working Group 3. Systolic and diastolic left ventricular function in children with primary hypertension: a systematic review and meta-analysis. *J Hypertens*. 2023 Jan 1;41(1):51-62.
- Sinha MD, Azukaitis K, Śladowska-Kozłowska J, Bårdsen T, Merkevcicius K, Karlsen Sletten IS, Obrycki Ł, Pac M, Fernández-Aranda F, Bjelakovic B, Jankauskiene A, Litwin M; Prevalence of left ventricular hypertrophy in children and young people with primary hypertension: Meta-analysis and meta-regression. HyperChildNet Working Group. *Front Cardiovasc Med*. 2022 Oct 31;9:993513. doi: 10.3389/fcvm.2022.993513. eCollection 2022.
- Lucas I, Puteikis K, Sinha MD, Litwin M, Merkevcicius K, Azukaitis K, Rus R, Pac M, Obrycki L, Bårdsen T, Śladowska-Kozłowska J, Sagsak E, Lurbe E, Jiménez-Murcia S, Jankauskiene A, Fernández-Aranda F. Knowledge gaps and future directions in cognitive functions in children and adolescents with primary arterial hypertension: A systematic review. *Front Cardiovasc Med*. 2022 Oct 20;9:973793. doi: 10.3389/fcvm.2022.973793. eCollection 2022

Comorbidities

- Malgorzata Wojcik, Julio Álvarez-Pitti, Agnieszka Koziol-Kozakowska, Michal Brzezinski, Rosita Gabbianelli, Vesna Herceg-Cavrak, Elke Wühl, Ignacio Lucas, Dragan Radovanovic, Anette Melk, Beatriz Gonzalez Lopez-Valcarcel, Fernando Fernandez-Aranda, Artur Mazur, Empar Lurbe, Claudio Borghi and Dorota Drozd. Psychosocial and environmental risk factors of obesity and hypertension in children and adolescents -A literature overview. *Front Cardiovasc Med*. 2023. PMID: 38054100.
- Vallejo-Torres L, Gonzalez Lopez-Valcarcel B. Socioeconomic and contextual determinants of

the burden of disease attributable to metabolic risks in childhood. *Front Public Health*. 2022 Nov 8;10:1003737. doi: 10.3389/fpubh.2022.1003737. PMID: 36424975; PMCID: PMC9681493.

- Stabouli S, Erdine S, Suurorg L, Jankauskienė A, Lurbe E. Obesity and Eating Disorders in Children and Adolescents: The Bidirectional Link. *Nutrients*. 2021 Nov 29;13(12):4321. doi: 10.3390/nu13124321. PMID: 34959873; PMCID: PMC8705700.
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Lifestyle treatment

- Alvarez-Pitti J, Herceg-Čavrak V, Wójcik M, Radovanović D, Brzeziński M, Grabitz C, Wühl E, Drozd D, Melk A. Blood pressure response to exercise in children and adolescents. *Front Cardiovasc Med*. 2022 Sep 30;9:1004508. doi: 10.3389/fcvm.2022.1004508. PMID: 36247478; PMCID: PMC9561233.
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Dissemination

- Lurbe E, Mancia G, Drozd D, Erdine S, Fernandez-Aranda F, Litwin M, Sinha MD, Simonetti G, Stabouli S, Wühl E; HyperChildNET Members. HyperChildNET: A European Network. *Front Cardiovasc Med*. 2023 Feb 7. PMID: 36748460.

Special issue

HyperChildNET was contacted by *Frontiers in Cardiovascular Medicine*. The journal offered HyperChildNET the opportunity to guest edit on a new research topic. This was a great chance for

HyperChildNET to increase the public visibility of our Action and to publish recent results of the project. The title of the research topic was 'Blood Pressure in Children and Adolescents: Moving Forward'. In fact, by September 2024, the total views of the special issue are 18,450. This high number confirms the interest in the topic and the Action itself.

Joint statement

The Joint STATEMENT FOR ASSESSING AND MANAGING HIGH BLOOD PRESSURE IN CHILDREN AND ADOLESCENTS TARGETING PRIMARY CARE PAEDIATRICIANS has been published in *Frontiers in Paediatrics*, the official journal of the EAP at the time of publication. The statement aiming to increase the implementation of the Guidelines [3] has 2 chapters prepared in a very practical way with schemes, tables and with a link to 3 free online calculators for helping paediatricians and professionals working with children to a rapid assessment of BP categories.

- Lurbe E, Mancia G, Calpe J, Drozd D, Erdine S, Fernandez-Aranda F, Hadjipanayis A, Hoyer PF, Jankauskiene A, Jiménez-Murcia S, Litwin M, Mazur A, Pall D, Seeman T, Sinha MD, Simonetti G, Stabouli S, Wühl E. Joint statement for assessing and managing high blood pressure in children and adolescents: Chapter 1. How to correctly measure blood pressure in children and adolescents. *Front Pediatr*. 2023 Apr 11;11:1140357. doi: 10.3389/fped.2023.1140357. PMID: 37138561; PMCID: PMC10150446.
- Wühl E, Calpe J, Drozd D, Erdine S, Fernandez-Aranda F, Hadjipanayis A, Hoyer PF, Jankauskiene A, Jiménez-Murcia S, Litwin M, Mancia G, Mazur A, Pall D, Seeman T, Sinha MD, Simonetti G, Stabouli S, Lurbe E. Joint statement for assessing and managing high blood pressure in children and adolescents: Chapter 2. How to manage high blood pressure in children and adolescents. *Front Pediatr*. 2023 Apr 12;11:1140617. doi: 10.3389/fped.2023.1140617. PMID: 37124176; PMCID: PMC10130632.

So far, the statement has been very successful with more than 5,500 views and downloads from all over the world. Interestingly the top countries with interest of the Statement are the USA, China, India, Germany and Spain, showing the interest and the utility of the Statement.

Tools

- *Website Portal*

From the very beginning and looking for a space to disseminate the project, an official website was created *to raise awareness* about the importance of BP in youths among health care professionals and, on the other hand, *to disseminate* healthy practices for the general population, with a particular focus on youths as well as their families and educators. The main objective is to improve the children's and adolescents' quality of life providing an Online Observatory with valuable and easily accessible material such as an e-book and fact sheets for target groups and stakeholders worldwide. To make the diagnosis of blood pressure categories faster and easier for physicians, free online calculators are available which use automated algorithms based on European guidelines for office, ambulatory and home BP.

The visually attractive and user-friendly website is the tool to advertise the announcement of meetings organised by HyperChildNET, the launch of all kinds of grants, it is the platform where video recordings covering the main topics are released.

HyperChildNET's official website is the tool where one of the landmarks of HyperChildNET, the European HyperChildNET week, has been disseminated. From 2021, the European HyperChildNET week which annually conveys its activity and future prospects to be developed. The week coincides with the World Children's day, 20th of November reaching professionals, families, children and adolescents looking for our objective to raise their awareness of Hypertension. A wide variety of dissemination and awareness actions are organised and to increase the dissemination, members of different countries collaborated to translate documents into their own languages and also to distribute dissemination materials among the target groups in hospitals and healthcare centres.

From the side of the industry, we would like to emphasise the cooperation with OMRON, a leading global manufacturer of blood pressure measurement devices. One example of the ongoing involvement of OMRON is the free online training course presented by the Vice-Chair of HyperChildNET Professor Elke Wühl and accessed for free from the website.

In September 2024, the website had received 92.000 visits with the higher number of visits from Spain, Poland and achieving the third position United States.

- *Calculators*

One of the most unresolved factors is the difficulty to define hypertension. Among others the large number of specific thresholds for the 95th percentile of SBP and DBP, resulting in large and complex tables whose use in the office during a childcare visit is time consuming, need to be highlighted. One step to solve this problem is to implement new tools, such as user-friendly calculators. In this way, HyperChildNET developed three free online calculators for office, 24-hour ABPM and home BP. The office and 24-hour ABPM calculators can be used as an instrument for paediatricians and other clinical professionals working with children and young people making a rapid assessment of BP categories. The need and the utility of these tools can be recognised looking at the number of visits that the calculators have received so far accounting to 42.000 coming from all over the world.

Cooperation with European scientific societies

One of the main tasks of the Action is to reach a wider audience including paediatricians, health care professionals working with children, families, children and adolescents and raise their awareness of hypertension. HyperChildNET aims for the achievement of compliance with the Guidelines among health providers. With this in mind, the Action established a very successful on-going collaboration with the EAP. The EAP was founded in 1961 and is a European professional association for paediatricians and acts as the paediatrics branch of the European Union of Medical Specialists. The EAP is the united voice of European Paediatrics and Child Health, representing 53 national paediatric societies across Europe and 14 European paediatric subspecialty societies, with close collaboration to a further 14 affiliated societies dedicated to Child Health.

From the very beginning members of HyperChildNET have been collaborating with the ESH, in fact many of them had already been authors of the ESH Paediatric Guidelines published in 2016. During the years of HyperChildNET, this cooperation has been maintained with presentations at the ESH annual meetings. Furthermore, more recently two members of HyperChildNET have contributed to the new 2023 ESH Guidelines for the management of arterial hypertension in adults (J Hypertens. 2023;41(12):1874-2071).

Promoting new networks of excellence

To generate new networks, HyperChildNET is expanding the already existing cohorts and team members,

setting up a new network association and creating a platform for network-based input to public policies.

In addition to the activities mentioned previously and considering that the first cause of hypertension in children and adolescents is obesity, HyperChildNET promoted a large-scale project within Horizon Europe. Focused on early prevention of obesity throughout the life course, eprObes 101080219 has been funded by the European Horizon Europe programme. This project was actively promoted by HyperChildNET and approved by the European Commission. This 5-year project has started in May 2023 with a budget of €9,875,000 euros. HyperChildNET has created a new network of Excellence.

Conclusions

HyperChildNET has become a solid and powerful network developing tools tailored not only at paediatricians and professionals working with children but also at families, health care providers, policy makers and stakeholders, and joining forces with scientific societies. HyperChildNET has been a platform for young researchers giving them the opportunity to network with leaders in the field, expanding their knowledge and leading to publications, another strength of the action. The Action has been holding dissemination and educational meetings, and furthermore awarding young researchers with grants such as STSMs and VMs.

Even though there is still a long way to go in paediatric hypertension, HyperChildNET offers a European perspective of the issue giving us the opportunity to develop new strategies and objectives moving forward in the field. A goal could be applying modern technology helping in the diagnosis and treatment follow-up and automatically transfer data from BP monitors to the calculators with the final destiny of the individual's health care record and potential development our calculators for mobile Phone application.

Authors' contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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