Network for blood pressure research in children and adolescents: A Cost Action

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Despite dramatic medical advances over the last few decades, cardiovascular disease (CVD) to which hypertension is the major contributor, remains a leading cause of death globally and the number one cause of death in the European Union, accounting for 42%. Although most of the adverse outcomes occur in adulthood, it has become clear that high blood pressure (BP) is a life course problem that can become evident in early life. Although 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. 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 healthcare systems, keeping people active and healthy.

COST ACTION: THE CASE OF HYPERCHILDNET

The European Cooperation in Science and Technology (COST) is a funding organization for the creation of research networks, called COST Actions. These networks offer an open space for collaboration among scientists across Europe and beyond, and thereby give impetus to research advancements and innovation.

The *HyperChildNET* (Network for BP research in children and adolescents) COST Action (Ref. CA19115) is a multidisciplinary network with participants from Europe, focusing on the urgent topic that is high BP, starting activities in October 2020 and extend during 4 years. The COST Action will promote coordinated and collaborative activities on personalized preventive measures for children and adolescents across Europe. The core of *HyperChildNET* is formed by a group of researchers pertaining to the 'Working Group on Hypertension in Children and Adolescents' of the European Society of Hypertension who has been working together developing the previous European Society of Hypertension (ESH) Guidelines in children and adolescents [1,2], with the involvement of other experts in the field.

COST Action will contribute pioneering research going beyond the state of the art and facing the most critical challenges affecting high BP in children and adolescents. *HyperChildNET* will go beyond the Working Group during its 4-year duration by:

1. Providing a multidisciplinary and multiactor approach, as it involves industry, stakeholders, target (patient) groups, researchers and clinicians in the networking actions.
2. Widening its scope with more ambitious goals taking into consideration a holistic approach of all the variables involved in BP regulation in children and adolescents.
3. Generating many networking actions not addressed by the ESH Working Group, such as short-term scientific missions, training schools, regular open seminars and global dissemination actions.
4. Enlarging the community through the involvement in *HyperChildNET* of world-leading researchers together with Early Career Investigators across Europe and other international partners.

THE CHALLENGE

The scientific and clinical community, as well as the decision-makers, stakeholders and the overall society, must face

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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 summarized as follows.

Assessment of hypertension prevalence in Europe

Since the 1970s, the prevalence of hypertension in children has increased nearly four-fold. It is estimated that the prevalence of hypertension in American and European children are 3.5% USA, 2.2–4.9% central Europe and 9–13% South and West Europe [3].

Definition of hypertension

The definition of hypertension 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 paediatric 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 hypertension 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 healthcare of children and adolescents. Two new guidelines have been published over the past 4 years [2,4]. Both agree on a number of issues but differ on several aspects that impact to a nonmarginal degree on clinical practice, that is the BP threshold that defines hypertension, 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 hypertension 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. So, the development of precise BP measurement protocols, assessment of hypertension 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 blood pressure 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. 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 hypertension-induced organ damage.

Validation of blood pressure 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 hypertension. In the last 3 decades, prestigious organizations, such as the US Association for the Advancement of Medical Instrumentation (AAMI), the British Hypertension Society, the 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 standardize 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 [5]. 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

Apart from 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 hypertension, 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 hypertension are not effective enough. 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 hypertension targeting at its origins or before sustained damage evolves. However, it is important to realize that successful prevention not necessarily avoid events, but usually delays them until a later time. Furthermore, the relevance of perinatal

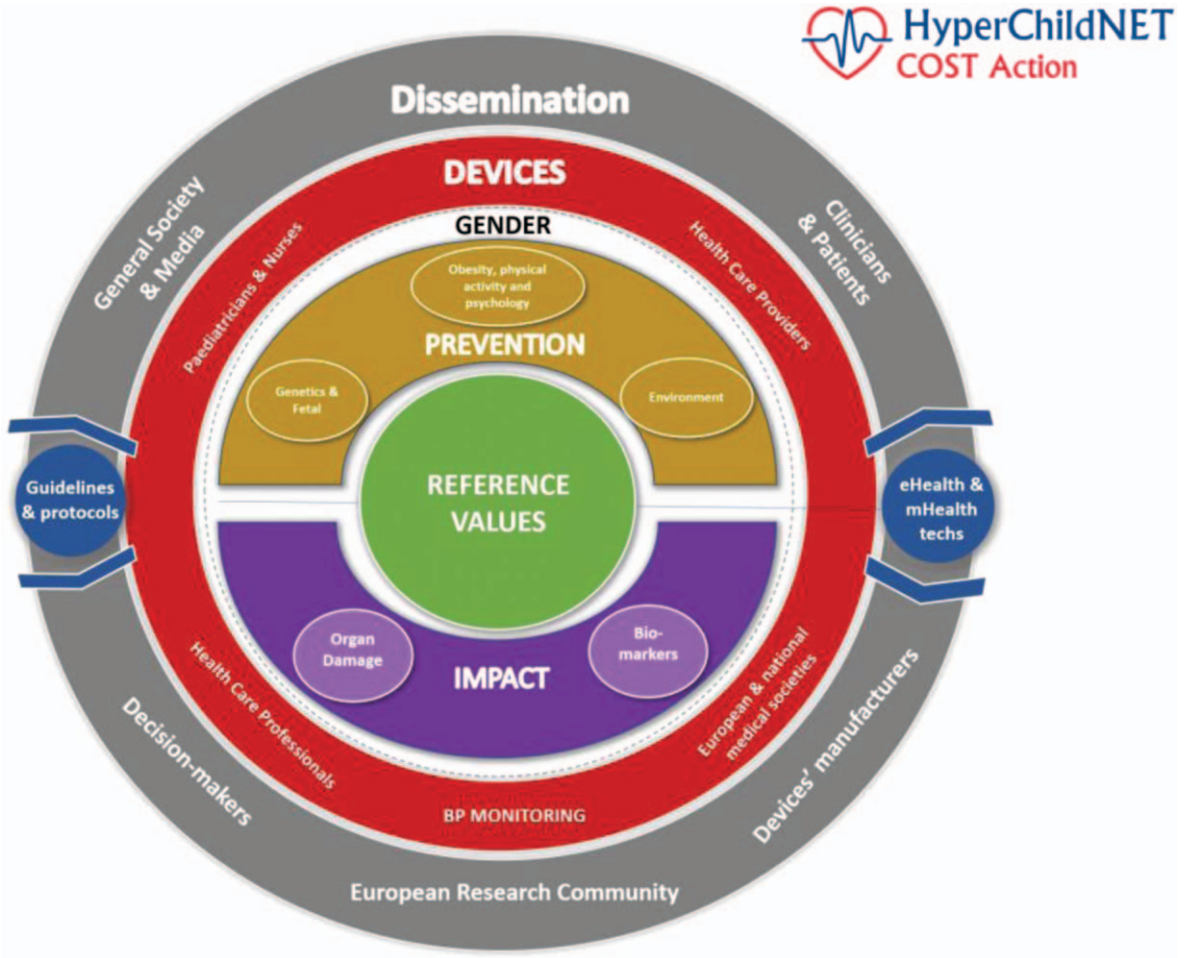

FIGURE 1 Visual summary of multivariable interaction in *HyperChildNET* networking.

programming opens up new ways to understand the early-life origins of diseases such as high BP. Understanding the interactions among genetics, foetal, environmental, psychosocial and psychological factors in the development of high BP is critical.

MULTIVARIABLE INTERACTION IN *HYPERChildNET* NETWORKING

To go ahead with this challenge, specific objectives have been developed and an ambitious master plan will guide concerted activities to be developed in the scope of an integrated multivariable action and interdisciplinary collaboration is shown in the Fig. 1.

APPROACH TO THE CHALLENGE

Progress beyond the state-of-the-art

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 organize 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.

Although hypertension has long been considered a disease of ageing, its prevalence is increasing in children and adolescents. 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.

Despite the body of emerging evidence, paediatric hypertension 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 healthcare burden and economic impact. Given that children with high BP are

likely to become adults with high BP, with all the attendant hypertension-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.

Added value of networking

In the present situation, high BP in children and adolescents is related to a wide range of variables, internal and environmental, modifiable and nonmodifiable, 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 proposed by Early Career Investigators. The network of Proposers is formed by experts bringing together the required competences and perspectives needed for the successful implementation of Working Groups to reach the expected goals.

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, healthcare providers, schools, parents, caregivers and society as a whole. *HyperChildNET* addresses 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.

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Conflicts of interest

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