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Policy Brief

"PRIMARY PREVENTION AS AN ESSENTIAL FACTOR ENSURING SUSTAINABILITY OF HEALTH SYSTEMS: THE EXAMPLE OF CONGENITAL ANOMALIES"

D. Taruscio[1], E. Bermejo-Sanchez[2], P. Salerno[1], A. Mantovani[3]

[1]*National Centre for Rare Diseases, Istituto Superiore di Sanità, Rome, Italy*
[2] *Instituto de Investigación de Enfermedades Raras (IIER), ECEMC (Spanish Collaborative Study of Congenital Malformations), Research Center on Congenital Anomalies (CIAC). CIBERER (U724). Instituto de Salud Carlos III, Madrid, Spain*
[3]*Department of Food safety, Nutrition and Veterinary public health, Istituto Superiore di Sanità, Rome, Italy*

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PRIMARY PREVENTION IN PUBLIC HEALTH

Since Hyppocrates, public health care means that, besides treating disease when it happens, science and actions should reduce the occurrence of diseases. This is specifically called "prevention". Primary prevention includes the actions aimed at preventing the onset of the disease. It results on eradicating, eliminating or minimising the impact of disease and disability on the population, through interventions that are applied before there is any evidence of disease or injury, by controlling causative risk factors; the main focus are disease risk factors, in order to reduce the disease incidence. Reduced disease burden means improved life quality and working capacity, reduction of avoidable disabilities and mortality, and lower costs for diagnosis and treatments, among other advantages. Thus, strengthening primary prevention may make the healthcare system more efficient and sustainable, while providing significant benefits to society as a whole, apart from the individual tangible and intagible advantages.

The different and relevant disciplines and actors involved in primary prevention often tend to think and operate in silos, concentrating on specific determinants such as lifestyles or living environment. Indeed, the actual problems call for an integration and cross-fertilization among different expertise fields: for instance, communities with low socio-economic status are more prone to live in more polluted settings, with insufficient availability of green areas or healthy food purchases. Therefore, it is also important to gather accurate data that can be analysed wisely to avoid confounding and to properly assess possible interactions of different variables and linked factors. These accurate analyses will have an impact on the identification of risk factors and the delineation of primary prevention measures.

Also, although primary prevention makes the health systems more sustainable, and despite its recognized major role among public health actions, primary prevention paradoxically does not attract a corresponding fraction of resources devoted to health by policy makers. EU countries overall allocate less than 3% of healthcare expenditure, and as low as 1% in some countries, to primary prevention actions.

The reduction of risk factors for poor health outcomes may involve actions beyond the specific domain of healthcare systems. The capacity to fulfill the primary requirements (food security, housings), the quality and safety of living environment (air, water, food), the social environment (education, income, lifestyles), the decisions of policy makers (in what refers to resources devoted to health services) are determinants involved in increasing or reducing threats for health. In principle, policies should consider their potential impact on health and undergo "health-proofing", as recently implemented in Ireland and a few other EU Countries.

The assessment of healthcare policies should be more prevention-oriented. Effective prevention is evaluated on the basis of 'diseases avoided'. This means that fit-to-purpose sets of performance indicators and outcome measurements should be developed accordingly.

PRIMARY PREVENTION OF RARE DISEASES: THE EXAMPLE OF CONGENITAL ANOMALIES

Congenital anomalies (CA) represent an important fraction of rare diseases, and at the same time, most CA can be considered rare diseases, based on their frequency. Due to the critical role of non-genetic factors in their pathogenesis, CA are the main group of rare diseases in which primary prevention measures already have a beneficial impact. Indeed, since 2013 the European Union has endorsed a body of evidence-based Recommendations for primary prevention of CA; these recommendations may be relevant to other adverse pregnancy outcomes as well (prematurity, stllbirths, developmental delays and related disabilities), as non-genetic risk factors are frequently shared. The recommendations may even have a beneficial impact on parents' health, for instance by modifying lifestyles or adopting better protection in the workplace, The Recommendations discussed the different institutional and societal levels relevant for developing and implementing primary prevention strategies.

The importance of CA on public health is clear: CA represented the most important cause of death in countries with low and very low under-5 mortality; Disability-adjusted life-years (DALY) rates due to CA have increased lately; the Years Lived with Disability have increased for CA; terminations of pregnancy for CA were almost three times more frequent than infant deaths and stillbirths with congenital anomaly combined, and this affects the Global Burden of Disease figures and their interpretation.

The bullet points below summarize the main fields pertinent to primary prevention of CA, encompassing both health systems and policies in relevant fields:

- Actions to mitigate **low socio-economic status** and **poor education** might have an impressive impact on a number of critical determinants, such as lifestyles (tobacco smoking and alcohol drinking during pregnancy, among others), and unbalanced diet associated with the increased risk of overweight/obesity, which, in its turn, is a significant risk factor for CA.
- Lifestyles can partly be tackled by specific policies, whose effectiveness should be evaluated in the context of specific countries. It is critical to reduce the consumption of energy-dense foods and drinks, tobacco and alcohol: a combination of policy actions and individual empowerment, starting from school, seems a suitable general approach. For instance, in Italy smoking in public places, including the workplace, has been forbidden by law in 2003: the law, matched with publicly-supported anti-smoking advertising, has been received by society with a favourable attitude and has contributed to reduce the number of smokers and especially the environmental exposure to passive smoking. Indeed, as already pointed out, exposure to tobacco smoking is a a risk factor for CA and other adverse pregnancy outcomes.
- Low socio-economic status and poor education are associated with a reduced access to **correct information** about health-protecting and health-promoting behaviors, such as the periconceptional supplementation with folic acid, and preconception care.
- The schooling system can play a major role in reducing health inequalities due to different socio-economic status and promoting health awareness and empowerment. The promotion of **health literacy programmes** since primary school can support the adoption

of a healthy lifestyle from childhood; a timely empowerment during school age toward correct lifestyles and behaviors may significantly reduce the risk factors for CA in the next generation.

- Actions to control and reduce the exposure to pollutants in living environment, workplace and foods: the current EU regulations on **hazardous chemicals** (e.g., the REACH regulation) put emphasis on the identification and management of developmental toxicants. Full implementation of the EU regulations, currently the world's most advanced ones, calls for a balance between scientific evidence, a reasonable use of the precautionary principle and the necessary involvement of the industrial and agro-food sectors.
- Pollution is not evenly distributed throughout the EU population: a number of **areas** are **highly exposed** to releases from toxic industrial activities and/or chemical waste from different sources (e.g., petrochemicals or persistent and bioaccumulative –"legacy" – contaminants). In communities with higher exposure to these hazardous chemicals in living environment, congenital anomalies (together with other adverse reproductive outcomes) represent an important public health issue as shown, for instance, in Italy by Sentieri, a ISS-led project. CA are also a sensitive sentinel for environmental quality, due to the relatively short latency time and the high susceptibility of the intrauterine life to major toxicological modes of action, such as endocrine disruption.
- The majority of the EU population aged between 18 and 65 years spends over half of their lives at the **workplace**. Workplace represents a diversified environment where exposures through multiple physical, chemical and biological agents can occur: to date women at fertile age are involved in every job role in the EU. But importantly, also men can be exposed to these hazards in the workplace, and this means that their gametes will form and mature in such environment, what can have an impact on the risk for gene mutations as well as on fertility. Effective prevention and health monitoring interventions in the workplace should be achieved through the co-operative involvement of employers, workers, occupational health professionals and legislators. Health and societal policies should recognize the basic right for a workplace environment that minimizes the health risks for workers as well as for their offspring.
- Chronic diseases such as diabetes, infectious diseases such as rubella and the emerging Zika viruses, as well as the inappropriate use of certain drugs, such as antiepileptic drugs, among others, are recognized risk facts for CA. Such risk factors can be significantly mitigated by functioning and accessible **healthcare services**. Hence, actions of top relevance for the protection of the generation(s) to come include the **care for maternal chronic diseases** (e.g., diabetes, epilepsy), the deliverance of **vaccination programmes** (e.g., toward rubella) and the enforcement of **pharmacosurveillance programmes**. These measures are supported by **information services** where the different actors involved in primary prevention (health care professionals and lay people) can solve their questions on the different risks and possible measures. Such policies could also receive a significant support by fostering the consistent involvement of pharmacists and nurses.
- **Pre-conception care** is surely the most effective way to put in practice all the known measures for primary prevention of CA, adapting them to the specific characteristics of

each couple. Therefore, policies should put special focus on the establishment of services specifically devoted to this approach by which specific risk factors can be identified, the most appropriate measures can be adopted accordingly, the most convenient information can be provided (adapted to the specific characteristics of each couple of parents to be) by health care workers, and some preventive measures can be put in practice.

- **Pregnancy planning** is another pivotal issue, that should be promoted by all means.
- The inadequate **access to health services** may be a special concern for low-status population groups and/or groups considered as **"marginal"** (immigrants, gypsies and other social-cultural groups, isolated communities). The primary prevention of CA in such population groups may require, therefore, specific attention and *ad hoc* actions.
- Health systems include **data collection and surveillance**: CA and rare disease registries of adequate quality can provide a valuable support to prevention strategies, e.g., by allowing ad hoc studies in order to assess potential risk factors (maternal diseases, drug treatment, occupation, etc.) or preventive actions, e.g., the diffusion of periconceptional folic acid supplementation at the right timing and dosing.

PRIMARY PREVENTION AS AN ESSENTIAL FACTOR ENSURING SUSTAINABILITY AND RESILIENCE OF HEALTH SYSTEMS

In 2015, countries under the umbrella of United Nations adopted the 2030 Agenda for Sustainable Development and its 17 Sustainable Development Goals. Governments, businesses and civil society together with the United Nations are mobilizing efforts to achieve the Sustainable Development Agenda by 2030. Universal, inclusive and indivisible, the Agenda calls for action by all countries to improve the lives of people everywhere. In particular Goal 3 "Ensure healthy lives and promote well-being for all at all ages" specifically states "Ensuring healthy lives and promoting the well-being for all at all ages is essential to sustainable development.. Major progress has been made. However, many more efforts are needed to fully eradicate a wide range of diseases and address many different persistent and emerging health issues."

Primary prevention, therefore, clearly pertains to the domain of ***sustainability***.

Health system sustainability means that today's efforts to protect and promote health will not reduce resources so to jeopardize the future efforts to provide an equitable and functioning health system to the next generation(s). Hence, owing to primary prevention, the health system will be more sustainable for society. A science-based primary prevention will reduce the burden of chronic of disabilities related to CA (measureble as DALY). This is important also in an ageing society: following the paradygm of "Developmental Origins of Health and Diseases", an effective primary prevention in the early lifestages (starting from intrauterine life, and even preconceptionally) can improve the quality of life of the increasing aged population, and reduce the societal costs for long-term treatment and care of chronic, often invalidating conditions.

Sustainable development in the field of health is the goal of meeting the needs of the present without compromising the ability of future generations to meet their own needs. In the fields of food safety and environmental health, for instance, the phasing-out and replacent of hazardous

chemicals (such as mutagens, teratogens, endocrine disrupters) are actions that can reduce the burden of disease for generations to come, by enforcing a safer living environment today.
Besides sustainability, prevention may also involve the concept of ***resilience*** at different levels.
Resilience means to adapt the system to changes in order to keep it functioning. The system must be able to adapt effectively to changing environments and identify and apply innovative solutions to tackle significant challenges - shortages of expertise/resources in specific areas, unexpected surges in demand with limited resources. In other words, they need to build and maintain resilience. Emerging risks, presenting either as new hazards or as new aspects of recognized hazards, call for resilient responses: one example in CA field is the recently recognized teratogen Zika virus. Emerging risks make evident the need for the health system to be able to understand changes and to adapt/modify its responses accordingly. The World Health Organization has considered Zika virus as a case study for emerging risk challenge. European countries can learn from the experience of other regions on how to communicate about Zika and apply these lessons to the European context, as the possible scenarios of Zika outbreaks can show significant differences in terms of size, and composition of the population at risk, cultural and socioeconomic reality and preparedness and response capacity.
Primary prevention actions should be targeted based on scientific evidence. This statement should not hide the many uncertainties still existing. A few examples of gaps of knowledge that increase the burden of uncertainties on primary prevention actions of CA can be mentioned:
in the field of *health interventions*, the benefit-to-risk assessment of flour fortification with folic acid; in the field of *chemical safety* the possible role of developmental exposures to pollutants in the obesity/diabetes epidemics; in the field of *response to emerging risks*, the role of climate changes of emerging infectious agents (such as Zika virus) and the associated teratogenic risks; in the field of *safe use of medications* the assessment of possible risks derived brome the use of herbal drugs and other widespread “alternative” medicines, in relation to pregnancy.
On one hand, the recognized presence of significant gaps of knowledge cannot, by any means, hamper the enforcement of evidence-based actions here and now.
On the other hand, and importantly, prevention needs research and innovation. An uncertainty is a gap of knowledge that can impair the assessment of the benefits introduced by a certain action. Therefore, uncertainties have to be identified and characterized, in order to plan and launch relevant research activities. Recently, it has been stated that for better sustainability and usefulness, it is crucial to refocus and streamline surveillance activities, avoiding just a “recreational” data collection; this can turn the statistically significant results into clinically relevant data. And also, it has been recommended to perform a “triple surveillance”: surveillance of causes, of disease occurrence, and of health outcomes. This means that such integral surveillance can be a really effective tool for primary prevention of CA.

RECOMMENDATIONS AND HIGHLIGHTS

CA, which include an important fraction of rare diseases, are liable to risk reduction by means of science-based primary prevention. In order to achieve an effective primary prevention, the following general recommendations have to be taken into account:

- the professional education and training of all health professionals (not limited to physicians) should provide an adequate room to primary prevention from both the qualitative and quantitative standpoint; this should include epidemiology, social medicine, environmental health, food safety and nutrition, as these themes can be relevant to work of the majority of health professionals.
- EU Member States should consider the "health-proofing" of all their policies. As pointed out in the above paragraphs, side to the health system, primary prevention involves several other legislative, intervention and scientific domains.
- health is a fundamental human right; at the same time, it can be considered that the "investment" on primary prevention generates both tangible and intangible benefits. It has been said that the "early childhood development is a smart investment" and "earlier the investment the greater the return": investing in primary prevention is obviously the earliest possible investment.

In conclusions the considerations on CA as an example for primary prevention in rare diseases identify the following **highlights:**

1) Investing in primary prevention based on scientific evidence is one essential factor ensuring sustainability of health systems.
2) Primary prevention is a pillar of sustainable development of society; protection of the early development will support the health of next generation(s) through to full adulthood and ageing.
3) In regard of many risk factors (e.g. nutrition, lifestyles, pollution, infections, medications) CA (together with other adverse reproductive outcomes) represent both an important public health issue *per se* as well as an early indicator of public health risks.
4) Effective primary prevention requires an integrated "One Health" approach, linking knowledge and action pertaining to human health as well as to physical and social living environments. From the policy standpoint, joint budgeting mechanisms can be envisaged to sustain intersectoral actions, involving the policy domains of health as well as those, e.g., social affairs, education, agriculture, and/or environment.
5) EU Member States: should devote resources to strengthen registries, and other tools for systematic data collection and surveillance on CA, so as to better inform national prevention strategies.
6) Pillars of primary prevention include science-based risk analysis and surveillance of potential health-damaging factors, citizen's empowerment and education of health professionals.
7) Characterization of uncertainties that weaken scientific evidence should target research programmes aimed at supporting the scientific basis of primary prevention.
8) EU Member States should consider the health and equity aspects in all their policies (short, mid and lon term).

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