

# INVESTING IN THE FIRST 1000 DAYS OF LIFE FOR A HEALTHY FUTURE

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**TNO** innovation  
for life

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## INTRODUCTION

Investments in child health and wellbeing are necessary to ensure a healthy and productive adulthood, and robust communities and societies. In this paper, we will discuss the latest insights into child health and summarize how TNO contributes to a healthy start to life through a collaborative effort involving various sectors and disciplines.

What do we mean by health? In 1948, the World Health Organization<sup>1</sup> adopted the following definition of health: ‘a state of complete physical, mental and social well-being, not merely the absence of disease or infirmity’. At that time, this definition was revolutionary because it took into account somatic, psychological and social health. While these factors remain important, much time has passed without any change to the definition, and there has been growing criticism because it does not refer to the equilibrium of individuals within their environment. TNO has contributed its vision of health – considered as a dynamic process – to this global discussion. International consultation and meetings have resulted in a new definition of health: ‘*Health is the ability to self-manage, in the face of social, physical and emotional challenges*’.<sup>2</sup>

This definition aligns with TNO’s vision for health in general and child health in particular. In order to improve child health, it is important to understand that children simultaneously develop physical, intellectual, social and emotional capabilities. These developmental processes are interrelated, interdependent and mutually reinforcing. Child health and wellbeing can be positively influenced by concurrently addressing the basic needs of children. These are: good nutrition, a nurturing and safe environment, and the ability to adapt to their surroundings. Interventions aimed at ensuring these basic needs should take place as early as possible, even before conception, and continue until the age of two at least. This window of time is framed as *the first 1000 days*. There is increasing evidence that investments during this period will not only contribute to child survival but will also lead to the continued health and wellbeing of children and enhance their ability to thrive.<sup>3</sup>

During the first 1000 days, virtually all systems in the human body are in a process of continual development, including the regulatory circuits that determine the body’s responses to internal and external stimuli. Biological stimuli include those originating from microbes (including pathogens) that influence developing organs and immune systems. Environmental stimuli with a negative impact include parental substance abuse, parental depression and stress, lack of parental attachment and some obstetrical interventions.

Diet plays an important role in delivering crucial nutrients in the right amounts and at the right time. Both malnutrition and over-nutrition have a strong negative influence on growth and can cause the development of chronic or other diseases.

During the first 1000 days, the child’s body (the regulatory system) is trained to respond to stimuli, in varying degrees and during different developmental periods. This may optimize or compromise the child’s capacity for resilience and adaption, which in turn provide the foundation for lifelong good or compromised health respectively. Current research has shown how interventions during the first 1000 days can increase the odds of favourable child development.<sup>4,5</sup> Knowledge about this crucial period must increase and be translated into practice. It is therefore essential to work with parents and care providers who understand and recognize the investments needed to raise healthy children. In this document we will further describe how TNO contributes to this goal and how we envision continuing to innovate, research and implement activities aimed at achieving a healthy start to life.

## WHAT WE ALREADY KNOW AND WHAT THE CHALLENGES ARE

Over the past two decades, research in the neurobiological, behavioural and social sciences has led to major advances in understanding the conditions and factors that lead to a healthy and productive life.<sup>6,7</sup> We are starting to appreciate the importance of early life experiences, such as those related to the environment and nutrition, on the development of the brain and the functioning of the immune system, as well as the central role of attachment and parenting on the essential social skills needed to manoeuvre through life. In addition, evidence shows that the rates of return on investments made during the prenatal and early childhood years average between 7%-10% higher than investments made after this period.<sup>8</sup> In the light of this, why is more money allocated to disease-specific treatments later in life as opposed to prevention and treatment-oriented health activities during the 1000-day window of opportunity?

While there is no one-off answer to this question, we do know that a number of factors influence this situation:

- The broader issue of child health is compartmentalized into various disciplines and sectors, which do not have a natural history of collaboration.
- The true benefits of prevention are not easy to calculate in terms of cost effectiveness and cost benefits.
- Scientific advances in child health need to be implemented in practice and in a way that the benefits of these are clear not only to health providers and users of health services but also to all other stakeholders, including the funders of healthcare.

New evidence is strengthening the assumption that investing in the first period of life is a guarantee for health and productivity, not only for the current generation but also for future generations. With the trend towards ageing societies, this early investment is imperative to reduce the costs of healthcare in the future. This requires a concerted effort to generate more evidence, collect more data, inspire more collaboration, stimulate more commitment and guarantee more investment to achieve the end goal of a healthy start for a healthy future.



# THE BUILDING BLOCKS OF CHILD HEALTH

There is a growing body of knowledge and experience that can be summarized according to the domains and areas of work.

## GETTING NUTRITION RIGHT IN THE FIRST 1000 DAYS

Nutrition during pregnancy and the first two years of life provides essential building blocks for brain development, healthy growth and the formation of a strong immune system.<sup>9,10</sup> Although the health benefits of nutrients (such as proteins and amino acids) has been known for a long time, there is emerging evidence about the interaction between microbiota (the community of microorganisms in a given habitat)<sup>11</sup> and the rest of the human body. Research has shown that there are intimate interactions between human intestinal microbiota and intestinal tissues that determine the absorption of nutrients from food. Moreover, this gut activity has a more far-reaching effect on brain activity (gut-brain axis). The effect of nutrition is thus twofold. Specific nutrients can affect the human body directly, or can be metabolized by microbiota, affecting their composition and subsequently changing their interaction with the human body. Since individual variation in microbiota composition is great and widespread, individual differences in their dietary effects are partly caused by the individual's microbiome (the collective genetic information on the microbiota).<sup>12</sup> The study of nutrigenomics aims to unravel the epigenetic effects of the microbiome on nutrients. Modern personalized diet (nutrition) approaches attempt to alter microbiota composition and function to obtain specific health effects.

Human breast milk is an example of this twofold effect of nutrition. Breast-feeding is known to prevent several communicable and non-communicable diseases in infancy and adult life. These health benefits associated with breast-feeding might be due to the particular composition of breast milk (proteins and amino acids) but might also be partly explained by the epigenetic processes described above.<sup>13</sup> Once these mechanisms are better understood for specific communicable and non-communicable diseases, personalized nutrition approaches implemented during the first 1000 days could potentially benefit the child's health throughout their entire life.

## THE CRITICAL 1000 DAYS FOR MENTAL, EMOTIONAL AND SOCIAL DEVELOPMENT

Within a few months, the brain grows from a few cells to a very complex system. The rapid creation of brain connections shapes a baby's brain development, having a lifelong impact on mental and emotional health. Apart from the phenomenal physical development (hardware), the function of the brain is also dependent on experiences early on (software). Maternal stress can pass on a message of danger to the unborn baby resulting in a higher risk of premature birth, and social and emotional problems after birth.<sup>14</sup> Attachment (the bond a baby makes with its caregivers) is a powerful predictor of a child's later social and emotional wellbeing. Securely attached infants feel confident to function autonomously and have confidence in their social and other problem-solving abilities.<sup>15</sup> A poor ability to regulate emotions associated with insecurely attached children and adolescents make them more vulnerable to psychopathology in later life.

## SYSTEMS BIOLOGY AND ITS RELATIONSHIP TO CHILD DEVELOPMENT AND HEALTH

The systems biology approach attempts to understand developmental processes in the human body, including interdependences between different parts of the system (such as the gut-brain axis). This includes the microbial populations (microbiota) inhabiting different parts of the human body, and the importance of the human microbiome in health and disease.

Babies born by Caesarean Section (CS) have a higher risk of developing obesity, asthma and other ailments compared to children born vaginally.<sup>16</sup> These babies also have a different microbial community on their skin, in their guts and elsewhere. It is possible to alter the microbiomes of babies born by CS by swabbing them with microbes from their mother's vagina, but it is not yet known how this affects their microbial colonization and health development later in life.<sup>17</sup> By studying how women's microbial communities change during pregnancy, it may be possible to identify women at risk of preterm birth, and develop ways to prevent it or deal with its complications in newborns – possibly by using dietary changes to enhance the healthy microbes in the placenta, vagina or the mouth and gut.<sup>18</sup> Antibiotic usage, either during pregnancy or after birth, increases the risk of child obesity as well as many other diseases. It appears that, especially during the very early phases of development, the human system is very sensitive to disturbances that lead to changes in regulatory settings, potentially influencing lifelong health.<sup>19</sup>

## **NEW MODELS OF HEALTH PROMOTION AND HEALTH SERVICES**

With these rapidly changing insights, new models of healthcare service and delivery need to be simultaneously introduced.<sup>20</sup> These models need to empower parents to actively manage their own health and that of their unborn or newborn child. In order to achieve child health and wellbeing, health services and health providers must be able to encourage lasting behaviour change, stimulating parents to adopt a healthy lifestyle for themselves and their unborn or newborn children.<sup>21</sup>

## **STATISTICAL MODELLING AND DATA ANALYSIS**

Improving the health of any individual requires relevant, trustworthy and timely information on that person's expected future development, and on the effects of possible actions to prevent and/or treat abnormalities. The information needed to make personal recommendations for improving health is dispersed across different scientific and psychosocial disciplines. The knowledge is thus fragmented in nature, and sometimes contradictory. Currently, an increasing amount of individual health data is being collected and stored. With the development of relatively non-invasive data collection techniques such as implants and wearables, some body functions can now be continuously monitored. The quantitative methods needed to analyse, integrate and synthesize this kind of data in order to make recommendations for any given individual are still in the early stages of development. However, in the near future, these methods should allow us to monitor growth and development in early life, and detect signs of problems before they arise. Ideally, we would like to predict the individual's later health based on different interventions, and then choose the appropriate actions accordingly. An entire new class of matching algorithms is currently being studied and will make this possible. These methods search for 'similar' people, and create an intelligent synthesis from the health outcomes of those who are matched. Although the potential is great, what is currently needed is experience in the field to see what these prediction models produce in practice.





## WHAT WE CAN ACHIEVE

We can develop, inform and implement sustainable solutions that utilize the entire knowledge cycle, from fundamental research to implementation research, within the life course from preconception through to the second year of life, which will have long-lasting effects and improvements. This will involve overcoming single-issue thinking as well as following a continuum approach to child health. Paramount to success is the inclusion of strategies shown to be effective in changing the behaviour of parents leading them to embrace a healthy lifestyle.

## PARTNERS AND PLAN OF ACTION

Within the various departments of TNO there are already strong connections and collaboration with partner and other organizations that are essential to this proposed approach to child health. These include:

- Policymakers and decision-makers
- Healthcare implementers, including municipalities and other local organizers
- Healthcare providers (including professionals and branch organizations) and institutions providing healthcare
- Research and academic institutions
- Advocacy, consumer groups and network organizations
- Private and commercial sector
- Partners in international development



## UNIQUE CONTRIBUTION OF TNO

TNO is well positioned to contribute to improved child health by delivering the added value of a multisector, multidisciplinary and integrated approach. Some specific examples of TNO expertise with respect to knowledge areas are:

### NUTRITION

Breast milk has been shown over and over again to have greater health benefits than infant formula. One of the components which contributes to this difference is the presence of human milk oligosaccharides (HMO) in breast milk. TNO has shown that specific HMOs can modulate infant microbiota composition and can even compensate for the disruptive effect of specific antibiotics on microbiota composition.

### SYSTEMS BIOLOGY

We have shown that the microbiota composition in the nose of young infants (4-6 weeks of age) determines the respiratory health of these infants up to the age of two, distinguishing between infants in a healthy and an unhealthy situation. This insight enables both the development of a novel diagnostic tool and the development of novel interventions.

### NEW MODELS OF HEALTH SERVICES AND HEALTH PROMOTION

- TNO has adapted the CenteringPregnancy™ group model of antenatal care specifically to the Netherlands, which combines medical check-ups with health information and the integration of three important components of healthiness: self-management, knowledge transfer and group support. To date, this has been implemented in more than 50 midwifery practices and the preliminary results are positive.
- Health promotion is only as effective as the degree of behaviour change that follows, and TNO has a track record in behaviour change methodology. An example of this is a successful web-based application combined with educational modules on occupational health for school level youth, addressing family planning and a healthy lifestyle before and during pregnancy.
- TNO has completed a successful pilot of CenteringParenting, testing a new model of delivering Preventive Child Health Services (based on the above-mentioned CenteringPregnancy™ model) that empowers parents through a group process that combines child check-ups with health promotion and information.
- TNO has developed iGrow™, a smartphone application for parents to track the development and growth of their child.
- TNO has developed new statistical methods and tools to predict the growth and development of individual children through simple measurements. The tools will also enable us to develop intelligent systems that alert and monitor individual growth and development.
- TNO is developing a digital platform for Preventive Child Health Service providers that will assist them in providing personalized support and care for every child they see.
- TNO has developed the 'doctor's bag', a combination of non-invasive antenatal diagnostic testing instruments with a clinical decision-making application which the test results are fed into, enabling the timely detection of complications by the healthcare provider and the appropriate treatment and/or referral required (specifically designed for developing countries).

### ATTACHMENT

- TNO has developed a Practice Guideline on problematic attachment relationships for professionals in Child Protection and Child Welfare Services. The guideline provides evidence-based information and practical recommendations, with TNO currently involved in training professionals in this field.
- TNO is involved in a study to test the validity of a simple instrument (LSVG) to screen young children on attachment security, comparing this with a well validated, more complex instrument (Attachment Q sort).

### STATISTICAL MODELLING AND (BIG)DATA ANALYSIS

- TNO has created a simple and robust scale of child development (D-score) combining physical, emotional and communication indicators to detect developmental delay in infancy. This has been developed for the Dutch Preventive Child Health Services and has the potential to be applied in other settings and countries.
- TNO has pioneered new statistical models to understand the effect of interventions at the individual level.
- TNO is an international leader in missing data methodology. These models form the scientific and computational backbone for synthesizing personalized recommendations in child health, and for harmonizing the vastly incomplete linked data sets found in practice.

## TNO'S VISION FOR THE FUTURE

Recent advances in science have started a revolution enabling the collection of an immense body of individual-specific information that needs to be translated and integrated into the healthcare system. By combining the knowledge of various sectors and disciplines and collaborating with the users of and providers in the healthcare system, we can contribute towards the further development of personalized health that in turn will lead to a better start in life and lasting positive health for children.

### NEAR FUTURE SCENARIO: TNO'S EXPERTISE IN PRACTICE – SARA'S CASE

Looking at the first 1000 days, we might follow the life of Sara as an example. Of course, Sara knows that choosing healthy parents is the first step towards lifelong health. While genes are unchangeable, epigenetic factors are influenced by lifestyle choices and environmental factors, which will influence her future health and that of other offspring in her family. Therefore, optimizing the health of future parents should be an important goal of any child health, nutrition and lifestyle programme. By implementing innovative do-it-yourself measurements of health that offer a thorough insight into daily habits and attitudes, combined with innovative IT, Sara's parents were given effective and personalized advice to stimulate healthy behaviour, before, during and after pregnancy.

After Sara's conception, her mother attended CenteringPregnancy™, a group model of prenatal care where the health information her mother received was given by her peers as well as the health professionals. The group model provided Sara's mother with peer support, gave her tips and the tools needed to approach Sara's birth and her parenthood without stress and empowered her to make good decisions about Sara's health and wellbeing. During Sara's birth, the birth team of professionals took into consideration new insights into microbiota and all measures were taken to not intervene with the normal process. When Sara needed a caesarean section to be born, she received the best possible personalized microbiota from her mother's vaginal swab to give her the same chances of development as her cousin Daan, who was born vaginally. One of the healthy choices Sara's parents made for her was to breast-feed, ensuring that Sara received the nutrients that would satisfy her personal needs. Sara's mother embarked on breast-feeding with confidence because she had made a well-informed choice and was supported by her husband, her parenting group and her healthcare professionals. Being a first child, Sara's parents were sometimes anxious about her health and development. Luckily, Sara's parents could rely on the user-friendly iGrow™ digital platform to not only monitor Sara's growth but also the healthy development of resilience and cognitive abilities. Sara's parents felt reassured that the same information was digitally available to their health professionals, who used it to provide tailor-made advice. In addition, Sara's physical, cognitive and emotional development was checked regularly using simple tools and checklists based on pooled data from many children such as Sara. When the time came for Sara to start eating solid foods, her parents were supported in this process through transparent information about What?, How? and Why? in a practical guideline co-developed with health providers.

From before her conception until she reached the age of two, Sara's health and wellbeing were important, not only to her parents and health providers but also to other stakeholders involved in the health sector (municipalities, politicians, insurance companies) and they all contributed to Sara being raised to be a happy and productive person.

TNO has experience with and expertise in a multisector, multidisciplinary and integrated approach to generating and transferring information and setting up the infrastructure that is needed for smooth alignment between all the stakeholders. This is important when all goes well and essential when something goes wrong, especially when the healthy future of Sara and thousands of other children is at stake.



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