Centre for Community Child Health

The First Thousand Days

AN EVIDENCE PAPER – SUMMARY

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The First Thousand Days: An Evidence Paper – Summary

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Executive summary

The earliest stage of human development – the period from conception to the end of a child's second year – has become known as the first 1000 days. Due to the significance of this period for future health and developmental outcomes, there has been a growing focus on the first 1000 days by governments, the early years sector and some commercial organisations.

Despite this growing focus, the Australian public's understanding of the significance of the first 1000 days is limited, and the policy response to date has not been in line with the weight of the evidence. As a result, the Australian Research Alliance for Children & Youth (ARACY); Bupa Australia; the Bupa Health Foundation; the Centre for Community Child Health at the Murdoch Children's Research Institute (MCRI); and PwC Australia formed a partnership with the aim of growing a greater awareness of what happens during the first 1000 days and why it matters, and facilitating evidence-based action on policy, practice and parenting.

One of the key deliverables of the Partnership's first project – **Strong Foundations: Getting it Right in the First 1000 Days** – is the compilation of *The First Thousand Days: An Evidence Paper*[1]. The aim of the Evidence Paper is to provide a comprehensive summary of the evidence for the significance of the first 1000 days. In keeping with the broad definition of health adopted by the World Health Organisation (WHO), which defines health as 'a state of complete physical, mental and social wellbeing and not merely the absence of disease or infirmity', the Evidence Paper examines the impact of early experiences on all aspects of development and functioning; including health and wellbeing, mental health, social functioning, and cognitive development. The Paper also recognises that, as enshrined in the United Nations Convention on the Rights of the Child, children have the same fundamental human rights as adults to a high standard of health and wellbeing.

This abridged version of the Evidence Paper summarises the key concepts outlined in the full paper; namely, the evidence for the biological, global, social, ecological, and individual factors that are reshaping our understanding of the first 1000 days.

The evidence is now clear that the way humans develop is a result of the interaction between a variety of genetic, epigenetic, and environmental factors that operate as an integrated system. This means we are not predetermined by any single factor; but rather from a mix of what we inherit from our ancestors and the contexts in which our development takes place. This is an important message, because it can help us resist the illusion that we have no control over who and how we are. What we do ('we' being individuals, families, communities, services and governments) matters.

Research is starting to uncover the mechanisms by which experiences during the early years affect outcomes. We know that experiences and environments can embed biological changes in children's bodily systems. We are starting to understand how the human being's capacity to adapt to its immediate environment by making changes to bodily systems can increase the risk of negative outcomes if the adaptations are not conducive to long-term health and wellbeing. And we are starting to appreciate how risks can escalate over time; with early adverse experiences and outcomes increasing the risk for later adverse experiences and outcomes.

With so many variables affecting children's health and wellbeing outcomes, it is realistic to assume that improving outcomes for all children, but particularly those experiencing the most challenges, will require long-term vision and commitment. Change is not impossible, however, and there is sufficient evidence to guide action.

Reducing health inequities and ensuring the best start to life for everyone, irrespective of socioeconomic status, race, or gender, must be an ethical and economic imperative for all governments. In addition to the immense personal and community costs, chronic diseases are also responsible for substantial economic burden given their collective impact on health-care costs and loss of productivity.

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1 For the full, referenced version of the Evidence Paper, see: Moore, T.G., Arefadib, N., Deery, A., & West, S. (2017). *The First Thousand Days: An Evidence Paper*. Parkville, Victoria: Centre for Community Child Health, Murdoch Children's Research Institute.

Action must primarily focus on two areas: education and empowerment; and changing the environment. Education and empowerment means taking a public health approach to supporting the public to understand the significance of the first 1000 days, and encouraging them to act to change their behaviours within the scope of their capacity to change, and with the resources available to them. At the same time, efforts must be made – at an individual, community, and societal level – to change adverse environmental factors that affect the broader conditions under which families are raising children.

In order to translate the evidence base into tangible actions, we need to achieve consensus across the sector for the changes that should be prioritised. To that end, we intend to use the *First Thousand Days Evidence Paper* as a foundational paper to underpin discussions at policy forums in late 2017 on the implications of the evidence.

Key messages

- During the first 1000 days, the developing foetus and infant are at their most adaptable, but also their most vulnerable. Starting from conception, the foetus is actively responding to changes in the environment, using cues provided by the mother's physical and mental state to 'predict' the kind of world they will be born into and altering their bodily structures accordingly. This powerful capacity is a double-edged sword; adapting to adverse experiences may help in the short term, but have negative implications in the long-term.
- The mind, brain and body function as an integrated system, and what happens in one bodily system affects all others to some extent.
- The range of factors now known to affect biological and developmental functioning during the first 1000 days is considerable. Some predate conception, including genetic and epigenetic transmissions from parents and grandparents; others occur during pregnancy, including maternal stress and nutrition; and still others occur during infancy, including neglect or abuse.
- Changes or adaptations made during the first 1000 days can have lifelong effects. Adult conditions such as coronary heart disease, stroke, diabetes, and cancer are now being linked to pathways that originated prior to or during the first 1000 days.
- Our physical and social ecology has dramatically altered over the past 60 or so years. This has changed the conditions under which families are conceiving and raising children, and has had a direct effect on their capacity to care for their children. This is because parental and family functioning – and therefore, children's development – are ecologically shaped.
- While much of the economic, technological and health developments have been beneficial, they have had unintended consequences that we are now beginning to recognise. These range from alterations to the composition of our microbiomes, which play an important role in maintaining health and wellbeing, to the growth of social inequities.
- Modern living conditions fail to provide the kinds of normal stressors that our bodies need to develop in a healthy way. As a result, we are subject to a wide range of 'mismatch' physical and mental health conditions, many with origins in the first 1000 days. These include allergies and obesity.
- Transgenerational transmission of risk factors can mean that some children inherit non-genomic changes that place them at greater risk of disease and other developmental problems.
- The problems resulting from the rapidly changing social context are complex and cannot be resolved by traditional governance or leadership models or by service-driven approaches.

- New knowledge is emerging about the underlying mechanisms by which experiences shape biological and neurological development; including changes at the cellular level (telomeres), biological level (epigenetic processes), neurological level (synaptic growth and pruning), and the microbiome level. However, as yet, we do not know how to intervene directly with these mechanisms.
- A key question concerns how permanent or otherwise these biological and neurological changes are. While we do not yet have the full story, we are starting to understand that some changes are partly or largely reversible through changes in the environments, while others may leave lasting effects. Some changes also have 'sleeper' effects, where they may only be detectable many decades after the precipitating experience.
- Some severe disturbances (such as schizophrenia) require a double or triple 'hit' of experiences or exposures before they are triggered.
- Children exposed to adverse environments and experiences early are likely to continue to be exposed to such experiences, which has a cumulative effect. In this way, a poor start to life in the first 1000 days may be the start of a cascade of events that reinforce earlier neurological and biological adaptations.
- What is undisputed is that reversing early adverse adaptations or inheritances gets progressively harder after the first 1000 days. While it is never too late to make changes, the first and best opportunity we have to build strong foundations for optimal development is during the first 1000 days.
- This review summarises a vast amount of cross-disciplinary research. Given the wide range of disciplines involved, interdisciplinary research should be encouraged, and ways of integrating research findings explored.

Background

This summary of *The First Thousand Days: An Evidence Paper* was produced as part of the **Strong Foundations: Getting it Right in the First 1000 Days** project. The Strong Foundations project is funded by the Bupa Health Foundation and is being delivered through a partnership between the Australian Research Alliance for Children & Youth (ARACY); Bupa Australia; the Bupa Health Foundation, the Centre for Community Child Health at the Murdoch Childrens Research Institute (MCRI) and PwC Australia.

The partnership was formed in response to the limited policy focus on, and public understanding of, the first 1000 days; the period from conception to the end of a child's second year. The partnership's key objectives are to:

1. raise greater awareness in policymakers of the importance of the first 1000 days; elevating the first 1000 days as a key issue for all levels of Government, and ensuring that policies and investments are based on the best available evidence
2. raise greater public awareness of the first 1000 days; to influence support for required policy and practice change, as well as informing and supporting caregiving/parenting practices
3. create a united, evidence-based narrative about the importance of the first 1000 days across the early years sector, including within practitioner and community groups, to help stimulate public and policy discourse and prompt action.

The Evidence Paper[2] establishes a foundation for the partnership's key objectives. We intend to use the Evidence Paper to bring together experts, policymakers and practitioners to discuss the implications of the current evidence and propose solutions and actions to advance as a united early years sector.

Scope of the paper

The Evidence Paper examines the impact of early experiences on all aspects of development and functioning, including health and wellbeing, mental health, social functioning and cognitive development. This is in keeping with the broad definition of health adopted by the World Health Organisation (WHO), which defines health as 'a state of complete physical, mental and social wellbeing and not merely the absence of disease or infirmity'. In Australia, Aboriginal and Torres Strait Islander people extend the concept of health to incorporate 'not just the physical wellbeing of the individual but the social, emotional and cultural wellbeing of the whole community'.

The paper also recognises that, as enshrined in the United Nations Convention on the Rights of the Child, children have the same fundamental human rights as adults to a high standard of health and wellbeing. The Committee on the Rights of the Child, charged by the United Nations with promoting and monitoring progress towards world-wide implementation of the Convention, provides General Comments to guide governments in fulfilling their obligations under the Convention. These include General Comment No. 7 (2005), on implementing child rights in early childhood, and General Comment No. 13 (2013), on the right of the child to the enjoyment of the highest attainable standard of health. The Evidence Paper seeks to identify the underlying determinants of health, so that children's rights to high standards of health and wellbeing may be better fulfilled.

2 For the full, referenced version of the Evidence Paper, see: Moore, T.G., Arefadib, N., Deery, A., & West, S. (2017). *The First Thousand Days: An Evidence Paper*. Parkville, Victoria: Centre for Community Child Health, Murdoch Children's Research Institute.

Introduction

The first 1000 days

The earliest stage of human development — the period from conception to the end of a child's second year — has become known as the first 1000 days. The recent and growing focus on the first 1000 days is due to a mounting body of evidence which shows the significance of environments and experiences during this period.

Our bodies develop and function in an integrated manner, with the brain intricately connected to other major bodily systems, including the immune, endocrinal, metabolic, cardiovascular, and muscular and skeletal systems. These systems shape and are shaped by each other. As Dr Tim Moore has noted, 'framing brain development in terms of building neuronal connections and brain architecture fails to capture the fact that brain functioning is not purely cognitive, that 'learning' is not purely conscious, that the brain is not purely skull-based, and that the brain is closely linked with other key bodily systems'.

This integration of bodily systems means that what is 'learned' in the prenatal and first two to three years of life has potentially profound consequences throughout the life course. Many challenges faced by adults, such as mental health issues, obesity, heart disease, criminality, and poor literacy and numeracy, can be traced back to pathways that originated in early childhood.

To ensure positive health and wellbeing for current and future generations, we therefore need to focus on improving the environments and experiences of the earliest stages of development, including the prenatal period. But where specifically should we be investing our efforts to ensure children receive the best start in life?

In the following sections, we will look at the current evidence on the factors reshaping our understanding of the significance of the first 1000 days. These can broadly be categorised as:

- Biological factors, including developmental plasticity and the developmental origins of health and disease (DOHaD) paradigm
- Global factors, including social climate change and the 'mismatch' hypothesis
- Social determinants of health
- Ecological factors, including the impact of child characteristics, the family, the community, and the environment
- Individual factors, including maternal, paternal and grandparental health and wellbeing.

We will then discuss the implications of this evidence for the action that governments, communities and the general public need to take to ensure all children have the opportunity to develop to their full potential.

Biological processes shaping health and development

Research shows that brain functioning is not purely cognitive, that 'learning' is not purely conscious, that the brain is not purely skull-based, and that the brain is closely linked with other key bodily systems. First, our emotions directly influence the functions of the entire brain and body, from physiological regulation to abstract reasoning. Second, many of the most important aspects of our lives are controlled by reflexes, behaviours, and emotions learned and organised outside our awareness. Third, the brain is not just skull-based, but 'embodied', being shaped by messages from all over the body via the central and peripheral nervous systems. Finally, the brain is not a stand-alone bodily system, but is intricately connected to other major bodily systems that shape and are shaped by each other, and function as an integrated mind-brain-body system.

Developmental plasticity and the developmental origins of health and disease

Developmental plasticity

One of the most significant features of human biology is our capacity to adapt to different social and physical environments. This capacity is known as *developmental plasticity*, and is at its greatest in the first 1000 days or so. During this time, there are brief critical periods in which systems and organs have to mature. Adapting to the immediate environment is the major developmental goal or activity during this time, therefore the influence of the environment is particularly critical.

The first 1000 days is also a sensitive period for the brain and central nervous system; a time window during which the effect of experience on brain development is remarkably profound and can strongly shape the neural circuits. This particular form of developmental plasticity is known as *neuroplasticity*, and refers to the biological capacity of the central nervous system to change structurally and functionally in response to experience, and adapt to the environment.

Two central mechanisms underlie this adaptation process: epigenetics (whereby the 'genes listen to the environment') and synaptic pruning (whereby the 'brain listens to the environment'). In both cases, developmental experiences and the social context in which they occur have the capacity to become biologically embedded (that is, have the capacity to alter human biological and developmental processes), with lifelong impacts on health and other outcomes.

Biological embedding

Adaptation involves a process variously known as biological embedding, through which the foetus (and infant), in response to cues such as nutrition or hormones, adapt their phenotype to their particular environment in ways that have lifelong consequences.

Two central mechanisms underlie this adaptation process: epigenetics (whereby the 'genes listen to the environment') and synaptic pruning (whereby the 'brain listens to the environment').

Epigenetic effects

The first key mechanism underpinning biological embedding is *epigenetic change*. Contrary to common understanding, genes do not single-handedly determine any of our characteristics. Instead, development is a dynamic process that involves interplay between genes and the environment. This means that, rather than being born with a fixed genome[3], we are born with a developing genome that changes in response to the environmental context.

Epigenetic changes have been implicated in the development of a wide range of disorders, from cardiovascular disease to autism spectrum disorders and cognitive disorders, and may be triggered by a wide range of environmental exposures and experiences. There is now also evidence that epigenetic changes may be inherited. This means that the experiences of mothers or even grandmothers can be transmitted across generations and contribute to the non-genomic transmission of disease risk across generations.

Telomere effects

Recently, a specific form of epigenetic change – *telomere effects* – has been identified. This demonstrates how experience is biologically embedded at a cellular level. Telomeres are the caps at the end of each strand of DNA that guard our chromosomes, similar to the plastic tips at the end of shoelaces, and they play a vital role in determining our health and longevity.

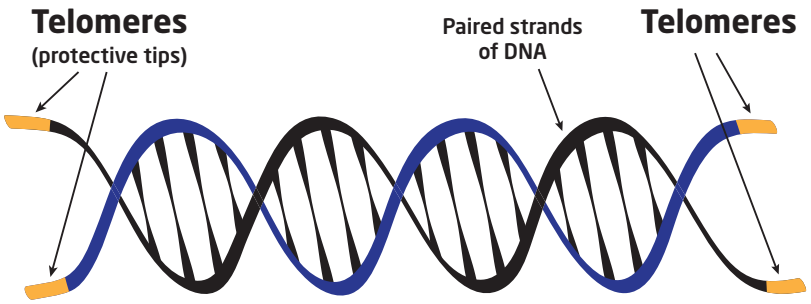

Figure 1. Telomeres.

Shortened telomeres not only shape our *health-span* (how long we live a healthy life), but also our *disease-span* (how long we live with disease that interferes with our quality of life). Telomeres are shaped by our genes, but also respond to how we live – the foods we eat, our responses to emotional challenges, the amount of exercise we get, whether we were exposed to childhood stress, and even the level of trust and safety in the neighbourhood.

Telomere length can be directly transmitted from mother to child at the point of conception: if the mother's telomeres are short throughout her body (including those in the egg when she contributes the egg), the baby's telomeres will also be short. The developing child's telomeres can be further shaped by the mother's nutrition and stress levels during the pregnancy. Fathers can also transmit shortened telomeres, although not to the same extent as mothers. Fortunately, telomeres can be lengthened through exposure to positive environments, so the impact of early adverse experiences or inheritance can be counteracted.

3 The genome is an organism's complete set of DNA, including all of its genes. Each genome contains all of the information needed to build and maintain that organism. In humans, a copy of the entire genome is contained in all cells that have a nucleus

Synaptic pruning

The second mechanism whereby environmental experiences become biologically embedded is *synaptic pruning*. While a baby is born with billions of brain neurons, it has relatively few synapses[4]. However, an initial surge in synaptic connections between brain neurons occurs after birth as the child goes through a process of rapid learning.

During this period billions of neurons in the brain send electrical signals to communicate with each other, and it is these connections that become the foundation of brain development. Connections are strengthened through recurrent use, while our experiences and environment determines which connections are used most. Connections that are used more become stronger and enduring, while those that are not used become weak and eventually fade away through a process called *synaptic pruning*.

The primary way that these brain connections are reinforced and strengthened is through the child's interaction with his/her caregiver(s) through a process of 'serve and return'. Children pursue interactions through facial expressions, gestures, babbling, and words, and adults who are responsive 'return' these 'serves' with similar vocalising, gestures, and emotional engagement. However, if a caregiver's response is unreliable, inappropriate, or absent, this under-stimulation can disrupt the developing brain architecture and adversely affect later stages of development, learning, behaviour and health outcomes.

Overall, our capacity to adapt makes the human species simultaneously versatile and vulnerable. That is, changes made that are adaptive for the immediate environment can come with long-term costs, both psychologically and physically. This knowledge underpins the developmental origins of health and disease paradigm.

Developmental origins of health and disease

The Developmental Origins of Health and Disease (DOHaD) paradigm maintains that environmental exposures such as stress or undernutrition during critical periods of development can have long-term effects on health and wellbeing.

The DOHaD paradigm also maintains that instead of being passive during pregnancy, the foetus actively responds to changes in the intrauterine environment, preparing itself for the environment it 'predicts' it will be born into.

This process of *predictive adaptation* works in the interests of the foetus and infant when the antenatal and postnatal environments are both optimal and stable, as this ensures that any changes to the phenotype[5] do not compromise later health and development. However, when these environments are less than optimal and when the prenatal and postnatal environments do not match, *predictive mismatches* (discussed further in '*The mismatch hypothesis*') can occur.[6]

The next major body of evidence reshaping our understanding of early development relates to global changes that have occurred over the past half century or so, and the impact of these on health and wellbeing.

4 A synapse is what allows information to flow from one brain cell (neuron) to another.

5 Where the genotype represents the genetic makeup of an organism, the phenotype is the outcome of the interaction between the genotype and the environment, and is the organism's actual physical form and behaviour.

6 Other models of how the foetus adapts to changes in the intrauterine environment include the thrifty phenome hypothesis and the maternal capital hypothesis. Regardless of the form that adaptation takes, the end results are the same – long-term effects on developmental health and wellbeing.

Global factors influencing health and development

Social climate change

Over the last several decades we have experienced a series of social, economic, demographic and technological changes that are unprecedented in their rapidity and scale. These collectively constitute a form of *social climate change*. For example, there have been dramatic changes in employment opportunities and conditions for families, with more parents working full-time, in shift work, working non-standard hours or working longer hours. Unemployment and insecure employment is also a growing problem, and there are more children being raised in poverty. The search for cheap housing and secure employment has led to families moving away from the communities in which they were raised, leaving many families isolated and lacking supportive personal networks (extended family, friends or other families with young children). Tackling these complex (or 'wicked') problems requires new governance, leadership and service system models.

The mismatch hypothesis

Evidence is now accumulating that social and environmental changes can contribute to physical and mental health problems arising from a 'mismatch' between human evolutionary capacities and modern environments. There are two forms of mismatch that can result in disease: predictive mismatch and evolutionary mismatch.

As discussed in the previous section, *predictive mismatch* occurs when our bodies make adaptations based on predictions regarding the kind of environments we are going to be living in, and the environments do not match those predictions. *Evolutionary mismatch* occurs when our bodies encounter conditions for which they were not evolutionarily adapted. For example, by reducing or eliminating a number of the normal sources of stress that human bodies require for healthy development — such as extremes of heat and cold, and cycles of feast and famine, and exercise and rest — our bodily systems can fail to develop properly.

This mismatch between our evolutionary capacities and our modern living environments has led to a rise in non-communicable diseases (NCDs) – responsible for nearly two thirds of deaths worldwide. According to the Australian Institute of Health and Welfare, about half of all Australians have a chronic disease, and around 20 per cent have at least two.[7]

Mismatch environmental influences during the first 1000 days have been shown to affect our susceptibility to a wide range of non-communicable diseases and conditions in later life. These include allergies, immune and autoimmune diseases, neurodevelopmental and neurodegenerative diseases/dysfunctions, arthritis and osteoporosis, inflammatory bowel disease, some cancer types, infertility, changes in timing of puberty, depression, and psychiatric disorders such as schizophrenia. Other evidence suggests that mismatch diseases can also result from the impact that changed living conditions have had on the human microbiome.

7 These calculations are based on the incidence of eight chronic diseases: arthritis, asthma, back problems, cancer, chronic obstructive pulmonary disease, cardiovascular disease, diabetes and mental health conditions.

The role of the microbiome

The microbiome is the collective name for the vast numbers of bacteria, viruses, and fungi that live in and on the human body. The microbiome plays an important role in our immunity as well as our ability to combat disease.

The genes that are transmitted from parents to infant are predominantly microbial. Only 1 per cent of genetic transfer is human, with the genes of microbes – the 'second human genome' – making up the rest. Any change in the abundance or composition or diversity of these micro-organisms can have significant health consequences. For instance, it may lead to failures to regulate and restore appropriate immune and inflammatory responses, which can contribute to chronic and inflammatory conditions such as inflammatory bowel disease and even psychiatric disorders such as depression.

Exposure to environmental and human microbiota is equally as important for optimal health and development. However, both have become less diverse as a result of modern lifestyle changes. Urban environments, higher exposure to chemicals and less exposure to green spaces, means that we have reduced contact with a diverse range of plant, animal and microbial life. The loss of microbial diversity is also due to overuse of antibiotics (in treating humans and in promoting the growth of the animals we eat), overuse of caesarean section births when not strictly necessary, the widespread use of sanitisers and antiseptics, and the shift to a Westernised high-fat high-carbohydrate high-fructose diet.

The developing immune system appears to be particularly susceptible to modern environmental change, contributing to the rise in two of the most common and earliest developing non-communicable diseases; allergies and obesity.

Allergies

Australia has one of the highest rates of allergic diseases in the world, with the latest generation of infants experiencing an epidemic of potentially life-threatening food allergies which were uncommon in their parents and rare in their grandparents. Research shows that the very early postnatal period is a critical time for immune development and allergy prevention. The gut, previously viewed as purely a digestive tube, is now known to be an immune organ which houses the largest immune network in the entire body. In the days following birth, there is an enormous influx of bacteria in an infant's gut, which stimulates the local immune system and the processes that prevent bacteria from 'infecting' or 'invading'.

Progressive modernisation and cleaner living appear to have altered the balance between humans and their friendly gut microbes. This has been a strong element in the 'hygiene hypothesis', which proposes that there may be an association between the change in exposure to microbes and the increased incidence of allergies. Infants who go on to develop allergic disease are known to have lower levels of 'friendly' bacteria in the first week of life, and higher levels of disease-producing bacteria. Newer studies also show reduced diversity of the gut bacteria in infants who go on to develop allergic disease. Collectively, this evidence strongly suggests that the pattern of colonisation of bacteria in the first few weeks of life may influence the patterns of immune development in later life.

Obesity

Childhood obesity rates have been described as reaching epidemic proportions in recent times. Excessive weight gain in infancy is associated with persistence of elevated weight status and later obesity, which has additional negative flow-on effects for children and adults alike. Some of the key prenatal influences on the development of childhood obesity include the mother's smoking habits during pregnancy; the mother's weight gain during pregnancy; and the mother's blood sugar levels during pregnancy – particularly, whether she develops pregnancy-related (gestational) diabetes.

However environmental influences do not stop with birth. Instead, they simply shift from a small, confined space largely controlled by the mother's genes, lifestyle, and physiology, to an unbounded environment with equally influential effects. There are three variable postnatal factors during infancy that impact weight in later life: how rapidly an infant gains weight, initiation and length of breastfeeding, and the duration of infant sleep. The first two of these factors (rapidity of infant weight gain and initiation and length of breastfeeding) are discussed further in *Nutrition in infancy*.

In relation to duration of sleep, studies have found that the association between restricted sleep and weight gain in adults may also hold true for infants. In a study of 915 children, infants who slept fewer than 12 hours a day were twice as likely to be overweight at age 3, compared with infants who slept more than 12 hours a day.

Early life holds the keys to how and why allergies and obesity develop, and is the best opportunity to reverse these epidemics. Thus, in considering environmental factors that may be driving the rise in these diseases, we must particularly consider their effects in pregnancy and the early postnatal period.

Social determinants of health

The next body of evidence shaping our understanding of how early development affects health and broader life outcomes concerns the social determinants of health: the social, economic, and environmental conditions into which we are born, grow, live, and age. Starting in the first 1000 days, our social determinants have the power to shape our lives for better or worse, unilaterally assigning us to a social standing that affects our economic resources, status and autonomy. Social determinants play a critical role in the first 1000 days, as it is during this period that a number of vital skills and abilities develop.

Social gradient effects in health and wellbeing

Research shows that the lower a person's social standing in life (e.g. persistent unemployment or chronic homelessness), the worse their health and wellbeing outcomes are likely to be. This global phenomenon is referred to as the social gradient in health, and it occurs from the very top of the socioeconomic spectrum to the very bottom. It is impossible to effectively address existing social gradients in health without also addressing the social determinants of health.

One of the most noteworthy social determinants of child health and wellbeing is poverty.

Poverty[8]

A significant body of evidence highlights the strong correlation between poverty in the first 1000 days and adverse health and wellbeing outcomes in later life. A recent American study found that areas of the brain responsible for learning, memory, and regulation of stress and emotions were connected to other parts of the brain in a 'weaker' way in children from low income families, as compared to children from higher income families. Moreover, research shows that while children from high income families with developmental delays are likely to catch up to their peers in later life, children of low income families are much less likely to do so and in fact, the gap between them and their more affluent counterparts is likely to grow exponentially.

While persistent poverty in the first 1000 days has been shown to have a cumulative negative impact on development, prolonged poverty during later stages of life is less likely to have a significant impact on future life outcomes. Moreover, relieving poverty (particularly in the first 1000 days) has been shown to increase birth weight and other outcomes, which can reduce the likelihood of negative outcomes in later life.

Poverty in pregnancy and infancy

Poverty in pregnancy is associated with a range of factors shown to increase the likelihood of health and developmental vulnerabilities in children, including increased use of tobacco, alcohol and other drugs, and poor nutrition and obesity. Poverty is also likely to increase a mother's exposure to psychological stressors, such as domestic violence and homelessness, which affects the body's normal regulation of hormones during pregnancy and increases the likelihood of foetal growth delay and preterm birth. However, women in the most economically disadvantaged areas of Australia are less likely to receive antenatal care in their first trimester of pregnancy, compared to women in the most economically advantaged areas.

8 Here, the terms 'poverty', 'low income' and 'economic hardship' will be used interchangeably.

Research into the influence of poverty on child development has primarily been guided by three key theories:

1. That economic hardship can contribute greatly to psychological distress in parents and hence negatively affect their caregiving capacity.
2. That families with greater financial resources have the capacity to make greater investments in the development of their child, whereas disadvantaged families may only be able to invest in the child's more immediate needs.
3. That children who are born into (and have a prolonged experience of) poverty are more likely to experience prolonged stress.

There is evidence for each of these theories, and the link between poverty in infancy and adverse outcomes in later life may be a product of all three pathways. While much has been learned, we have yet to fully understand the relative strength of these different influences or how they fit together. Further research is needed to settle these questions.

Aboriginal children experience poverty at significantly higher rates than their non-Aboriginal counterparts, and this is only one of a number of social determinants that inequitably affect Aboriginal people.

Social determinants and Aboriginal[9] health

Aboriginal parents have strong cultural practices in family life and child rearing, and know how to keep their children safe and to raise them to be active contributors to family and community life. However, the effects of intergenerational trauma, cultural disconnection and family disruption among many Aboriginal communities, are increasingly being recognised as factors which can have significant adverse outcomes for some Aboriginal children.

The social determinants of Aboriginal health include (but are not limited to) social status, employment, poverty, housing, education, the experience of racism, and intergenerational trauma. While all of these factors have a disproportionately large impact on the health and wellbeing of the Aboriginal population, a growing body of evidence highlights a significant relationship between a robust affinity with traditional cultures and improved health and wellbeing outcomes amongst Aboriginal peoples.

Aboriginal children experience poverty at significantly higher rates than their non-Aboriginal counterparts and have some of the poorest health and developmental outcomes in Australia. While we know that the 'traditional' social gradients in health contribute significantly to the disparities between Aboriginal and non-Aboriginal children, there are additional factors (unique to the experience of Aboriginal Australians) that also play a contributing role.

One is that marginalisation and discrimination are often deeply embedded in the lives of Aboriginal people, limiting the likelihood of health benefits that are typically associated with improved income, education, etc. Another reason is that the generational marginalisation of Aboriginal people can impact optimal development in a number of ways, placing some Aboriginal children at a greater disadvantage from the beginning of life and limiting the acquisition of skills that can be drawn upon for the benefits of health at all levels of the gradient. Finally, kinship, spirituality, connection to traditional lands and cultural continuity play a central role in the health and wellbeing of Aboriginal Australians. However, these factors are not captured in our 'traditional' understanding of the social determinants of health.

9 In this section, the term 'Aboriginal' refers to Aboriginal and Torres Strait Islander Australians. Based on 2011 Census data, around 3 per cent of the Australian population (approximately 670,000 people) were estimated as being Aboriginal. Approximately 80 per cent live in urban centres on the east coast, while the remaining 20 per cent live in small towns and remote communities across the tropical north of the country and through the Central and Western deserts. The health and developmental outcomes for these two populations can differ significantly.

The historical and ongoing circumstances of colonisation and the profound and sustained marginalisation of Aboriginal peoples are credible explanations for a much less consistent social gradient within Aboriginal populations (Shepherd et al., 2012). Racism, materialised in the marginalisation of a group of people, is acknowledged as having a detrimental impact on the health of Aboriginal (and other minority groups) throughout the world. Moreover, the experience of racism[10] can restrict access to cultural activities, which are found to be protective factors for Aboriginal people's overall health and wellbeing.

The social determinants of health, particularly relating to poverty and the systematic discrimination of Aboriginal Australians, help us to understand the foundations upon which disparities in health and wellbeing outcomes of Aboriginal and non-Aboriginal children are formed. While there is limited evidence which directly relates to the social determinants of Aboriginal children health (particularly in the first 1000 days), the fact that Aboriginal children are significantly more likely to be born with low birthweight, amplifies the early start and consequences of socioeconomic disadvantage.

Much work is underway to redress inequities between Aboriginal and non-Aboriginal children. For example, The First 1000 Days Australia model, led by Professor Kerry Arabena at the University of Melbourne, is building a coordinated, comprehensive, culturally informed strategy to strengthen Aboriginal families to address their children's needs. This model incorporates a research program that is premised on culture being the main protective factor in ensuring the health and wellbeing of Aboriginal families.

10 Racism is conceptualised as comprising avoidable and unfair phenomena that lead to inequalities in power, resources and opportunities across racial or ethnic groups. It can be expressed through beliefs and stereotypes, prejudices and discrimination, and occurs at many social levels, including interpersonally and systemically, and as internalised racism.

Child, family, community and environmental factors shaping health and development

The next body of evidence shaping our understanding of the significance of the first 1000 days examines some of the primary child, family, community and environmental factors that influence development. These include child characteristics (such as temperament), the relational environment (such as parent engagement), and the physical environment (such as housing).

Child characteristics

Temperament

Temperament refers to individual differences in the regulation of experience which emerge early in life and remain moderately stable across development. Temperament can affect young children's mood and emotions, how they approach and react to situations, and their level of fear, frustration, sadness, and discomfort.

The influence of temperament on developmental pathways and outcomes is now widely recognised. For example, stressful family environments experienced in the infant's first year of life in conjunction with highly reactive, avoidant and impulsive temperament styles have been found to contribute to anxiety and depressive symptoms in children at 4 years of age.

The biological foundation of a temperamental bias (a bias towards certain temperamental characteristics) is usually, but not always, genetic. In some cases, it is the result of severe stress or infection in the pregnant mother. The behaviours in infants and young children that are most often attributed to a temperamental bias are unusually high or low levels of irritability, motor activity, smiling, ease of regulating these responses, and a consistent tendency to approach or to avoid unfamiliar people, objects and places. However, it is important to note that a temperamental bias does not determine a particular future trait: life experiences affect the bias and create a pool of possible personality traits.

Differential susceptibility

There is evidence to suggest that children differ in the extent to which they are influenced for better or worse by their environmental experiences, due to 'vulnerability' in their make-up. This vulnerability may be behavioural (e.g. difficult temperament) or genetic. Children with such 'risk' characteristics are thought to be disproportionately affected by rearing influences, including adverse experiences, while more likely to benefit from highly supportive environments.

Parental and family characteristics

Children's development is significantly shaped by the nature of their relationship or attachment with their primary caregiver during infancy. A consistently responsive and nurturing relationship between the child and its caregiver encourages a secure attachment and facilitates the development of future relationships throughout the child's life, while providing a secure foundation for learning.

Over the past decades, families have become much more diverse in their structure. Concerns about the possible impact of these new family structures on children's development have been proven unfounded. It is the quality of the parenting, children's own personal characteristics, and the social and physical environment in which children are raised that is important, rather than the way the family is constituted.

Neurobiology of interpersonal relationships

Temperament-related behaviour and parenting behaviour influence one another, and are independently associated with child socio-emotional development. Children's self-regulatory difficulties are more likely to lead to externalising problems when parents use inconsistent discipline strategies or are low in firm discipline.

The notion that infants with difficult temperaments may be more susceptible to the effects of parenting than infants with less difficult temperaments is consistent with the larger differential susceptibility hypothesis, which proposes that children may differ in the degree to which parenting qualities affect aspects of child development.

Parent-child attachment and parenting style

To learn effectively, children need to feel calm, safe and protected. When this attachment process is interrupted, the child's brain places an emphasis on developing neuronal pathways that are associated with survival, before those that are essential to future learning and growth.

Attachment research during childhood demonstrates that infants are born with a range of attachment behaviours that seek proximity to and safety in supportive others (attachment figures). Proximity and safety seeking is a way for the child to maintain or increase its positive feelings and minimise or regulate its stress feelings and defensive states. Although there are various sub-categories of attachment styles, they can essentially be broken down into two overarching styles: secure attachment; and insecure attachment.

Secure attachment is defined by a sense of attachment security, comfort with closeness and interdependence, confidence in support seeking, and other positive ways of managing stress. This occurs in infants whose caregiver(s) respond to their distress in a consistent, caring, and timely manner (e.g. picking up and comforting the infant). A secure attachment is aligned with enhanced developmental outcomes in later life in areas such as self-reliance, self-efficacy, empathy, and social competence.

Insecure attachment arises when caregivers are unavailable, unresponsive or unpredictable in responding to the child's needs, proximity seeking fails to relieve distress, and alternative strategies for emotional regulation (other than proximity seeking) are developed. Extended separation from the attachment figure leads to a sequence of reactions: an initial intense activation of the attachment system (including crying for and searching for the attachment figure); despair and apathy; and detachment (including avoidance of the caregiver, even on their return). However, despite this apparent lack of concern, infants with avoidant attachment patterns have been shown to have more physiological arousal than other infants, indicating that they have learned to supress their distress. Insecure attachments are often associated with an increased likelihood of developing social and emotional maladjustment in later life.

Parenting style in the first 1000 days is central to establishing the child's attachment style, and therefore health and wellbeing outcomes in later life. Parenting style relates to the emotional context that caregivers create to communicate with the child.

The three primary parenting styles – affection or warmth; behavioural control; and psychological control – have each been associated with varying child social and emotional outcomes. For example, warm, responsive and supportive parenting has been shown to promote the development of children's emotion regulation and social skills. However, negative parenting characteristics, including strictness, neglect, control, punishment, and lack of support will potentially lead to child behavioural and emotional problems in later life.

While research on parenting often focuses on the role of mothers or families in general, growing evidence supports the critical and unique role of fathers/male caregivers[11] in early childhood development. For example, evidence supports that fathers play a more prominent role in facilitating play exploration which fosters emotional and behavioural self-regulation, whilst mothers are more likely to provide comfort in times of distress. Moreover, research indicates that fathers play a distinct (as in different to mothers) role in children's socialisation. Specifically, fathers who model positive behaviours such as accessibility, engagement and responsibility contribute to: better psychosocial adjustment; better social competence and maturity; and more positive child/adolescent-father relationships.

Conversely, poor father-child relationships and fathering behaviours can have a lasting effect on a child's social adjustment and relationships, associated with inferior adult social functioning; significantly reduced likelihood of secure adjustment; and a significantly greater risk of avoidant or dependent attachment styles. Moreover, poor quality early father-child relationships have been associated with an increased likelihood of mental health disorders such as depression, bipolar, anxiety disorders and phobias in later life regardless of socioeconomic status and perceived quality of childhood maternal relationship.

Adverse interpersonal relationships and sustained trauma

While it is clear that positive health and developmental outcomes for children depend on caregiving that is responsive, warm and consistent, the evidence is equally as clear that unresponsive and harsh or punitive parenting in the early days is likely to result in adverse health and developmental outcomes throughout the life course.

Child abuse and neglect: an Australian snapshot

In 2014-15, 1 in 35 Australian children received child protection services, 73 per cent of whom were repeat clients with at least one previous case of child protection involvement. Infants (under the age of one) were the most likely age group to receive child protection services across Australia, while children who lived in the most disadvantaged areas of Australia (an overwhelming majority of whom were Aboriginal) were also more likely to receive child protection services than any other cohort.

There has been a consistent increase in the number of notifications and substantiations over the last five years, with a 6 per cent increase in the last 12 months alone. Alarmingly, research shows that these figures are likely to under-represent the number of child maltreatment (including fatal) incidents.

11 In the remainder of this section, 'fathers' will be used to mean fathers and male caregivers.

Adverse early life experiences and poor lifelong outcomes: the linking mechanisms

There are three mechanisms by which sustained exposure to abuse and/or neglect increases the likelihood of ill (physical and mental) health and early mortality:

1. By disrupting the progression of critical developmental processes (namely the stress response and brain development).
2. By affecting the way in which children relate to and interpret the world around them.
3. Through increased engagement in adverse health risk behaviours for physiological or psychological benefit (e.g. substance abuse as a coping mechanism).

For children who experience abuse and/or neglect, the ongoing 'wear and tear' on the body's stress response can seriously harm development, and ultimately, health and wellbeing outcomes. Over the last decades, overwhelming evidence has established a strong dose-response (response that varies based on levels of exposure) between exposure to adverse early experiences such as abuse and neglect, and increased likelihood of cognitive and language difficulties, lower educational attainment, unemployment, poverty, homelessness, becoming victims or perpetrators of violence in later life, early mortality, heart disease, diabetes, liver disease, cancer, depression, anxiety, eating disorders, obesity, and suicide.

Impact of family and domestic violence

Children do not need to be the recipient of physical or verbal violence to be affected by it. Overwhelming evidence supports the correlation between children's exposure to family and domestic violence and the increased likelihood of adverse lifelong outcomes. In one study, interpersonal conflict was the strongest risk factor for behavioural problems, significantly associated with externalising and internalising behaviours and social and attention problems, when children were assessed at the age of five. More frequent and intense episodes of inter-parental conflict also increased the likelihood of childhood behavioural problems.

Domestic violence in pregnancy and infancy

Pregnancy is recognised as a period of high risk for the onset or worsening of domestic violence. Pregnant women who are victims of domestic violence are more likely to experience all forms of violence, including physical assault, sexual assault, and psychological aggression. Violence during pregnancy can also be more extreme, posing a significant risk of harm to the mother and unborn child. High levels of maternal stress can result in an increase in the mother's cortisol production, which can enter the foetus' brain via the placenta or the umbilical veins, adversely affecting the growing brain. Maternal anxiety during the earlier part of the prenatal period is associated with lower birth weight, shorter gestational age and smaller infant head circumference at birth, suggesting a decrease in brain growth.

Studies have found a strong correlation between domestic violence during pregnancy and poor emotional regulation and academic outcomes in school, behavioural problems during infancy, poor maternal attachment, an increase in internalising problems from as early as 24 months, and aggressive behaviours at school.

Abuse during pregnancy strongly predicts abuse immediately following birth. Threats to a caregiver are one of the most psychologically destructive traumas for children. Infants who hear or witness anger and/or violence can show symptoms of Posttraumatic Stress Disorder, including eating problems, sleep disturbances, a lack of typical responses to adults, and loss of previously acquired developmental skills. They are also more likely to demonstrate greater child adjustment difficulties and increased externalising behaviours in later life including lower levels of social competence, difficulties with peer relationships, aggressiveness, and disruptive behaviour.

As we have seen, the experiences that a child has within their familial environment plays a fundamental role in shaping their future health and life outcomes. However, it is not the only factor that helps shape future outcomes. The community that a child grows up in and their physical environment (such as their housing conditions) are also extremely important in shaping their future health and wellbeing.

Community environments

Over the past few decades, communities in Australia and other developed nations have been steadily fragmenting, and people's sense of community has fragmented also. There are a number of reasons for this, including increased family mobility and the search for affordable housing. Continued population growth combined with the steady shift to cities is outstripping the capacity of cities to provide the basic physical and social infrastructure to adequately support families. Other contributing factors include increases in the speed and ease of transport and of communication methodologies that have enabled people to have contact with much more widely spread social networks, reducing reliance on people in the immediate neighbourhood.

These changes are important because both the social and physical environments of a community are known to affect people's health and wellbeing. There is evidence that our immediate social networks – those people we mix with on a regular basis – have a significant influence on our ideas, emotions, health, relationships, behaviour, and even our politics. Even 'consequential strangers' – people outside our circle of family and close friends, such as casual acquaintances – are important for personal and community wellbeing.

Social supports in pregnancy and infancy[12]

Social supports play a particularly significant role during periods of stress or major life transition. Pregnancy is a time of significant life change and requires psychological adjustment and support. Social supports during pregnancy reduce the likelihood of maternal stress, depression and risk taking behaviours during and after pregnancy. Conversely, the perception and experience of insufficient support has a visibly detrimental effect on not only maternal psychological wellbeing, but also adverse health and wellbeing outcomes for the child.

Social supports play a significant role in the health and wellbeing of children in a number of ways including:

- facilitating the child's contact with other caring adults who help build positive attachment relationships
- modelling relational skills for children
- improving parental caregiving capacity by promoting positive mental health and resilience during challenging periods
- reducing the likelihood of child maltreatment
- encouraging families to access family and/or early intervention services.

The changing nature of communities means that, for many families, their social supports may not be living in the immediate vicinity, and for some families, they may not exist at all. This is a significant risk factor for the health and wellbeing of both parents and children.

12 The terms 'social supports' and 'social connections' are used interchangeably and refer to three categories of family support: practical (having someone who can offer a lift, or help look after your child, etc.); emotional (having someone who will listen and provide emotional comfort and reassurance, particularly during a stressful situation, etc.); and advice and information (having someone to contact who can help and/or provide advice if the baby is not feeding/sleeping, etc).

Physical environment[13]

Research continues to demonstrate the direct (cognitive, social, emotional, and biological outcomes) and indirect (parents' caregiving capacity) effects of physical environments on children's development.

Housing[14]

Access to stable and adequate housing is a basic human need. It has a significant impact on the health and wellbeing of families and children as it provides a safe environment, autonomy, and security which is needed for full participation in social, educational, economic, and community life.

Research has linked negative home environments during the first 1000 days with a host of developmental issues, including (but not limited to): inferior language development; behaviour problems; insufficient school readiness; aggression, anxiety and depression; and impaired cognitive development.

Specific issues related to housing include:

- **Housing mobility**. The absence of a secure home can make it challenging for a child to establish a sense of identity and self-esteem. Children may experience difficulty establishing bonds (e.g. close friendships) that make them feel secure and develop healthy social habits. Continuous moving may change social connections by eliminating a family's close social networks that provide emotional support and information about the community.
- **Overcrowding**. Overcrowded housing can negatively affect children's sense of autonomy, social behaviour, health, developmental outcomes, and school performance. It can also affect their sleep patterns due to the different schedules of household members, and this can lead to difficulty concentrating during the day, and poor mood and behaviour. Children in overcrowded houses are also less likely to have sufficient space for play and may also experience greater risk of abuse due to the difficulties they face in removing themselves from potentially volatile situations. Moreover, when parents have to cope with overcrowding it affects their parenting behaviour and can lead to increased conflict between children and parents, as well as marital conflict.
- **Homelessness**. Homelessness is a complex problem that places children at increased risk of long-term poverty, homelessness in adulthood, unemployment, chronic ill-health, and other forms of disadvantage and social exclusion. One Australian study of homeless pre-schoolers reported that about 50 per cent of the study sample suffered significant emotional developmental delays. Compared with children from low-income households that have never been homeless, children from homeless families are twice as likely to be hospitalised and make significantly more visits to hospital emergency departments. A higher incidence of asthma and other respiratory problems, infectious diseases, trauma related injuries, lead poisoning, chronic diarrhoea, visual and neurological deficits, delayed immunisations, tooth decay, ear and skin infections, conjunctivitis, and mental health problems and behavioural disorders have also been found.
- **Housing quality**. While some exposure to dirt and bacteria is beneficial, excessive exposure to environmental allergens (such as mould) has strong and critical effects during infancy, and early childhood and respiratory health may be determined by such exposure during the first year of life. Poor quality housing is usually situated in neighbourhoods experiencing higher levels of poverty, and the risk factors associated with these neighbourhoods also contribute to unfavourable child outcomes.

13 Physical environment refers to factors such as housing, access to parks and safe places for play, access to green spaces and natural environments and level of road traffic at the expense of pedestrian safety and comfort.

14 Housing refers to a dwelling that is safe, secure, affordable, and appropriate. It also encompasses issues relating to housing mobility, homelessness, neighbourhood characteristics, and over-crowding.

Young children are particularly vulnerable to inadequate housing because they:

- are physiologically more susceptible to environmental hazards (e.g. mould and allergens)
- spend more time in the home and as such have more exposure to environmental hazards
- are more susceptible to physical features of a home that can cause injury
- have limited control over their environment.

Built environments

Over 90 per cent of Australians live in urban environments, and neighbourhoods are a key setting in which children begin their lives. To date, the evidence indicates that the way we design and build neighbourhoods can promote healthier lifestyles and contribute to reducing the risk of non-communicable disease. Features of the built environment that promote healthier lifestyles include easy access to facilities, services, social infrastructure, parks and recreational facilities, and stores selling fresh produce. Poorly designed neighbourhoods may have less connected street networks and limited access to shops and services, but an oversupply of fast food restaurants.

Natural environments

Increasingly, evidence shows that access to nature and green spaces provides children with various cognitive, emotional, and physical benefits, including (but not limited to): an increased ability to concentrate, better educational attainment, reduced stress and aggression, and lower risk of obesity. Green spaces have also been shown to increase social interactions between families and children, promoting social trust and community perceptions of safety.

Alarmingly, growing evidence depicts the correlation between poverty (and race) and the presence of environmental hazards and lack of access to the natural environment.

Environmental toxins

During the first 1000 days, humans are uniquely vulnerable to the effects of toxic chemicals in the environment. Early life exposures to toxic chemicals are important causes of disease and neurodevelopmental disorders.

Industrially applied or produced chemicals have been associated with neurotoxicity in humans and exposure to these modifying compounds, through consumer products or environmental pollution, poses serious threats to public health. Harmful exposures can start as early as in utero. Because of the omnipresence of chemicals in our daily life, pregnant women have continuous contact with chemicals in food, water, air, and consumer products. Despite the fact that the foetus is carried inside the mother's womb, the mother's chemical body burden is shared with her foetus; many substances easily cross the placenta and the foetal blood-brain barrier to reach the developing brain. As a result of these preconception and pre-birth exposures, the next generations are born "prepolluted". Evidence of these exposures comes from analyses of the umbilical cords of newborn babies showing they contain an average of two hundred industrial chemicals.

The brains of infants and children are uniquely sensitive to environmental neurotoxicants at levels far below those that are known to harm adults. The foetus' small size and immature state of development mean that it is more vulnerable to environmental toxins during the prenatal period than at any other time in its life. This is because they are exposed to larger doses relative to the body weight at a time when organ systems are being formed and rapid growth of neurological structures is occurring. Exposures to substances such as lead that have minimal or no discernible impacts in adults can permanently alter brain development and function in a child.

These chemical exposures, especially during critical and sensitive windows of development such as pregnancy, can contribute to preterm birth and lead to a myriad of health consequences that can manifest across individuals' lifespan, and potentially be transmitted to future generations. Based on a review of the evidence regarding a range of environmental toxins, researchers Heyer and Meredith estimated the period during which exposure to each toxicant was most likely to increase the risk of developing neurodevelopmental disorders such as ADHD, autism spectrum disorders, and schizophrenia. They found that the sensitive time-windows for the majority of toxicants occur between conception and birth, although children also continue to be vulnerable to toxin exposure post-birth.

Individual level factors influencing child health and development

The final body of evidence we will examine that shapes our understanding of the significance of the first 1000 days is that relating to individual factors. These include: maternal and paternal nutrition; breastfeeding and the introduction of solid foods; substance use; and stress.

Nutrition

There is now clear evidence that early life nutrition in the foetus, infant and young child can have profound effects on long-term health. From preconception to adulthood, our dietary intake has the ability to shape the individual or population health trajectories for better or worse. Over the past few decades, research has shown that good nutrition is central to optimal health and development outcomes and disease prevention. Conversely, excessive intake of energy or insufficient intake of protective nutrients, especially during critical periods of development, is associated with poor health and contributes to health disparities.

The presence or lack of good nutritional status of the mother and/or child is a critical factor in 'programming' the child for healthy development and positive long-term health and wellbeing outcomes. Foetal and early-life nutrition has been linked to setting the risk for conditions such as coronary heart disease, Type-2 diabetes, osteoporosis, asthma, lung disease and some forms of cancer.

Nutrition in preconception and pregnancy

It is well established that maternal nutrition can affect the offspring's epigenetic state and have lifelong effects on: children's mental health; food/flavour preferences; satiety; muscle mass; and insulin resistance. This is because the foetus uses nutritional input from its mother to anticipate the kind of nutritional world it will be born into, and adjusts its phenotype accordingly, as discussed in the section on *Developmental Origins of Health and Disease*.

Research shows that the developmental induction of risks in an obesogenic environment (environmental influences that promote obesity) is considerably influenced by maternal nutritional status at conception, during pregnancy, and during weaning. Women who are overweight or obese before pregnancy are at greater risk of developing hypertensive disorders such as pre-eclampsia during pregnancy, and giving birth to larger infants who are at increased risk of developing obesity in later life. Overweight and obesity can also increase the risk of stillbirth, difficult delivery, haemorrhage and birth defects.

Weight gain during pregnancy can also affect the immediate and future health of infants. While excessive gestational weight gain can increase birth weight and postpartum weight retention, inadequate gestational weight gain can increase the likelihood of poor foetal development.

Increasing evidence is also pointing toward a relationship between paternal obesity and adverse health outcomes in the offspring. Paternal obesity impairs sex hormones, basic sperm function, and molecular composition, which results in disturbed embryo development and health, and an increased offspring disease burden. However, some studies have shown that reversing obesity-inducing parental programming may be possible with diet and exercise interventions.

Nutrition in infancy

The speed of postnatal growth is at its highest during infancy – a time when the infant is entirely dependent on others to meet its nutritional needs. Inadequate nutrition and restriction of growth during this period can result in permanent stunting and contribute to lifelong deficits in neurological functioning. Excessive and rapid weight gain in infancy however, is also a concern and has been linked to obesity in later life, as well as a number of risk factors for cardiovascular disease.

Michaelsen and colleagues found that in the period after birth most infants, even the most vulnerable, grow and develop normally if they are exclusively breastfed. Exclusive breastfeeding has been shown to at least modestly protect against excessive early infant gain and later obesity, an effect that may result from differences in composition of weight gain between breastfed and formula-fed infants.

The method of infant feeding (i.e. suckled directly at the breast or via a bottle) can also affect infant growth patterns. When feeding at the breast, the pace and volume of intake are controlled by the infant, however the caregiver maintains more control when bottle feeding. Infants fed from a bottle (rather than breastfed) consume more milk, protein, and energy, potentially resulting in greater weight gain. Removing control from the infant may also affect the infant's ability to interpret satiety cues and self-regulate food intake accordingly. These mechanisms are thought to occur regardless of what is in the bottle (i.e. breast milk or formula).

A longer duration of breastfeeding has been associated with decreased likelihood of obesity in later life. Harder and colleagues found that the risk of obesity was reduced by 4 per cent for each month of breastfeeding, with this effect lasting up to a breastfeeding duration of 9 months. Breast milk has also been found to decrease the likelihood of developing allergies in later life as it contains many immune factors and substances that promote favourable colonisation of the gut with friendly bacteria.

Breastfeeding and introduction of complementary foods and drinks

Complementary feeding commences when breast milk alone is no longer sufficient to meet the nutritional requirements of infants. The timely introduction of appropriate complementary foods (at around 6 months, but not before 4 months of age) promotes the good health and nutritional status of infants during a period of rapid growth. If complementary foods or drinks are introduced too early or are not given safely in the correct quantity at the optimum time, growth rates can falter dramatically and lead to growth restriction and even stunting. Stunting is irreversible, and is associated with an under-developed brain.

Intergenerational effects of prenatal nutrition

The long-term consequences of adverse conditions during early development may not be limited to one generation, but may lead to poor health in the generations to follow, even if those individuals develop in normal conditions themselves.

Ongoing studies are contributing to an increasing understanding of how changes in metabolism and epigenetic regulation of gene expression caused by poor nutrition can be passed from one generation to the next. These models will eventually help us to understand the underlying mechanisms (physiological or epigenetic) behind the developmental programming of health and disease and shed light on the transmission of diabetes, obesity and cardiovascular disease.

Substance use

Alcohol

Exposure to alcohol in the uterus is the leading cause of cognitive impairment and neurodevelopmental disorders, and the most common preventable cause of birth defects. According to the 2013 National Drug Strategy Household Survey, over 50 per cent of pregnant women consumed alcohol before they knew they were pregnant, and one in four continued to drink once they knew they were pregnant.

The effects of alcohol on the embryo or foetus can produce a spectrum of disorders that affect physical, learning and behavioural outcomes. The range of effects is collectively termed 'foetal alcohol spectrum disorder' and can include abnormalities in the formation of the face, intellectual and learning disabilities, deficits in executive functioning, memory problems, speech and language delays, inattention, hyperactivity, internalising and externalising behavioural problems, and social impairments that remain to varying degrees throughout life.

There is inconsistent data about the effect of light alcohol consumption on pregnancy outcomes. However, based on available research evidence, it cannot be stated that light drinking in pregnancy has been established to be safe.

It should be noted that the co-morbidity of psychological ill health and presence of socio-developmental issues are critical to this area. Any guidelines on the management of alcohol use/misuse in the first 1000 days should reflect the multifactorial nature of this occurrence, rather than focusing solely on a cause and effect relationship between substance use and negative outcomes in the foetus and newborn.

Illicit drugs and other psychoactive substances

The association between substance abuse and adverse outcomes has particular implications for the unborn child. The prenatal effects of substance use in pregnancy include premature birth, foetal distress, physical and/or mental retardation, birth defects and withdrawal symptoms upon birth. Treatment resulting in separation could also have implications for infant-maternal attachment.

In the longer term, the effects of in utero exposure to drugs and alcohol include (but are not limited to) increased risk of sudden infant death syndrome (SIDS), impulsivity, learning disabilities, antisocial behaviour, and neurological deficits.

Australian research has shown that of the women seeking treatment for substance dependence, approximately half are mothers, and that poly drug use (two or more drugs used at, or near, the same time) is often the norm. These women also had a range of other co-occurring physical and psychological health concerns, including hepatitis, eating disorders, histories of self-mutilation, suicide attempts and low self-esteem.

It is well established that children who are raised in families with parental substance misuse often have poor developmental outcomes. However, parental substance abuse often co-exists with other risk factors (such as domestic violence, low income and transience) and it is the sum of these various influences that determines the child's lifelong outcomes.

When a parent is intoxicated, their ability to provide adequate care and protection to an infant is significantly compromised. Child death reviews conducted by the Victorian Child Death Review Committee have consistently noted the high prevalence of parental substance misuse among deaths of infants known to the Victorian Child Protection Service. This can result, for example, from substance-affected parents sleeping with infants.

Social isolation is a key feature of the lives of families with parental substance abuse. Typically, women with substance misuse problems feel unable to attend a range of community activities that are often the building blocks of community connectedness and support. Parents who have limited social support and live socially isolated lives are at greater risk for poor parenting practices. This is especially the case when these problems are further compounded by other risk factors, such as parental mental health problems and socioeconomic disadvantage.

Tobacco

There is conclusive evidence that smoking causes compromised fertility, and that parental smoking potentially has long-term and serious consequences for child health. Nicotine induces the narrowing of the blood vessels, which affects the function of the placenta, restricting blood flow and reducing the supply of nutrients and oxygen to the foetus.

There is also growing evidence that smoking during pregnancy affects the normal development of the brain systems that regulate oxygen uptake and heart function, increasing the risk of stillbirth, neonatal death and sudden infant death syndrome. Blood vessel constriction and high levels of carbon monoxide in the blood caused by smoking may induce hypoxia (oxygen deficiency), which has been implicated in placental abruption. Hypoxia can also result in the enlargement of the placenta, causing it to extend over the cervix, as seen in placenta praevia. There is also some emerging evidence for neonatal effects from nicotine withdrawal.

It is unknown as to whether pharmacotherapies such as nicotine replacement therapy are safe to use in pregnancy. Nicotine itself has the potential to disturb the development of the embryo or foetus and there is no known safe level of nicotine that can be administered during pregnancy. The Smoking Cessation Guidelines for Australian General Practice state that: "pharmacotherapy should be considered when a pregnant woman is otherwise unable to quit, and when the likelihood and benefits of cessation outweigh the risks of pharmacotherapy and potential continued smoking."

Mothers who smoke are less likely to start breastfeeding their babies than non-smoking mothers, and tend to breastfeed for a shorter time. Breast milk production is also lower in smokers than in non-smokers. Exposure to tobacco smoke during infancy has also been associated with slower rates of growth in lung function and increased risk of asthma, middle ear disease, and respiratory disease.

Stress

Researchers have consistently found that various types of chronic stress (otherwise known as toxic stress) are linked to — and probably cause — shorter telomeres. Telomere shortness and stress have independently been associated with several common conditions, such as cardiovascular disease and diabetes. Toxic stress during pregnancy affects the foetal nervous system and reduces foetal growth and length of gestation. Poor growth in utero is a major risk factor for a number of subsequent health problems in the child's later years, including: physical and neuromuscular maturation; behavioural and emotional development; and cognitive development.

Toxic stress can also affect a parent's caregiving capacity and risk taking behaviour, once the child is born. Failure to alleviate severe stress caused by prolonged threats such as violence, financial hardship, abuse and emotional neglect, particularly in children, will result in exponentially higher personal and economic costs further down the line.

Beyond the first 1000 days

Thus far, we have reviewed the evidence relating to the factors and mechanisms by which children's health and development can be positively or negatively affected. This section examines how children's experiences in the first 1000 days translate to outcomes in later life; and how long-lasting those effects are.

Pathways to later outcomes

There are four key ways in which early childhood experiences affect long-term outcomes. They are:

1. biological embedding
2. accumulation effects
3. developmental escalations of risk over time
4. triple hit effects.

Although they are distinguishable from one another, these pathways are not mutually exclusive.

Biological embedding

As outlined in the section on *Developmental plasticity*, a great deal has been learned about the mechanisms underlying the process of biological embedding (i.e. the capacity to alter human biological and developmental processes), and the role of epigenetics and of telomeres in particular. Understanding these mechanistic causes of developmental outcomes is important because it enables us to understand the causal chains whereby these outcomes are achieved. However, epigenetic changes by themselves do not determine our subsequent development any more than our genes do. While they increase the risk of poor health outcomes in later life, whether or not these risks lead to actual poor outcomes depends upon the context (e.g. exposure severity or length of time) in which they are embedded and the complex interactions with other experiences and environments.

Accumulation effects

Development is also shaped by the cumulative effect of experiences. Over time, the cumulative wear and tear caused by exposure to chronic stress results in physiological changes to the body with long-term adverse consequences for health and wellbeing.

This biological wear and tear eventually leads to maladaptive physiological responses that increase disease risk and undermine health. Childhood poverty may actually 'reset' the immune system in a manner that increases stress-related impairments in immune function, rates of infectious and chronic diseases, or blood pressure and cardiovascular disease incidence.

The 'Matthew effect' refers to a pattern of increasing advantage or disadvantage following early advantage or disadvantage. Because children's learning is cumulative, early functioning is predictive of later functioning. However, behaviour and functioning at any point in time are also more strongly influenced by the immediate social and physical environment than by past experience. The apparent contradiction between these two findings can be resolved by recognising that, for a variety of reasons, children's environments tend not to change. While this is not a problem if these environments are positive and stimulating, prolonged exposure to adverse environments can have adverse long-term effects upon children's development and learning.

Escalation of risks over time

Development is also shaped by developmental escalations in risk over time. An exposure or experience at one stage of the life course influences the probability of others later in the life course, as well as associated health and developmental outcomes. This is akin to the notion of chains of risk, whereby a sequence of linked exposures raises disease risk because one bad experience or exposure tends to lead to another. Such causal chains are common in living things and are known in biology as cascades:

> **Because our biological and psychological traits are caused by cascades of events, development can be understood as being the product of a history of cascading causes in which each subsequent change depends on prior changes.**

This sequential chain can also work in the opposite direction, such that some individuals experience 'positive cascades of development'.

All three of these concepts describing the pathways from experiences to outcomes — biological embedding, accumulation effects, and escalation of risks over time — illustrate the significance of prevention and early intervention; and signify that prevention and early intervention are the primary means to avoid or minimise adverse changes to bodily systems that can lead to future ill health.

Triple hit effects

The triple hit hypothesis combines elements of the three previous pathways, and helps explain why some people who experience adversities respond with resilience, while others develop stress-related physical and mental disorders. This pathway posits that three conditions or events are required to disrupt development: (1) an existing predisposition or vulnerability; (2) a critical period of brain development; and (3) exposure to environmental stressors. If only one or two of these conditions are present, the infant may be protected from the development of adverse conditions, or the conditions may not be as severe.

Measuring the cumulative effects of experiences and exposures

What all four pathways illustrate is that there is not a simple process whereby an experience or exposure at one point in time will lead directly to a developmental outcome at a later point. Development is contextual, and shaped by a combination of factors rather than any single factor.

To help understand and measure the cumulative impact of experiences and exposures, the concept of the exposome has been proposed. The exposome — including exposures from the environment, diet, behaviour and endogenous processes — is highly variable and dynamic, and evolves throughout the lifetime of an individual. Various exposome initiatives are currently being undertaken, and a proposal for a Human Exposome Project (as an environmental analogue to the Human Genome Project) has been put forward.

Long-term outcomes of early experiences and development

The evidence cannot tell us precisely how much of the non-communicable disease risk seen in ageing can be attributed to early life. What this review does is identify the first 1000 days as the period of greatest developmental plasticity, and has described the acute sensitivity of the foetus and infant to environmental experiences and exposures during this period. However, it is important to note that a degree of plasticity is retained over the life course. That is, epigenetic changes can be modified, and brains can be rewired, but it takes stronger and more sustained efforts to achieve this.

What this means is that we need to maintain support and provide appropriate intervention beyond the first 1000 days for those who have experienced a potentially compromised beginning to life. We also need to maintain a level of support for those who have experienced optimal beginnings, as positive early experiences do not 'inoculate' children against subsequent adverse experiences (although they can convey a greater level of resilience for when they may be confronted with later challenges).

Implications for action

Reducing inequities and ensuring the best start to life for everyone, irrespective of socioeconomic status, race, or gender, must be an ethical and economic imperative for all governments. In addition to the immense personal and community costs, chronic diseases, unemployment, welfare dependency and criminality are also responsible for substantial economic burden given their collective impact on health-care costs, criminal justice systems costs and loss of productivity.

Promoting 'optimal conditions' in early life is the best hope we have of hardwiring 'healthy' physiological, structural, immune, metabolic and behavioural-response patterns in order to prevent so many avoidable diseases. There are three distinct developmental periods during the first 1000 days when actions to promote better outcomes can be taken: preconception, pregnancy and infancy.

- **Preconception**. The evidence has highlighted the impact that the health and wellbeing of parents prior to conception can have on the foetus from the moment of conception. This is defined as a set of interventions that aim to identify and modify biomedical, behavioural, and social risks to a woman's health or pregnancy outcome through prevention and management. It is being advocated as a means to positively address the rising rates of adverse gestational and paediatric illnesses.
- **Pregnancy**. In this review of the evidence, the importance of development during the nine months in the womb has been highlighted again and again. The factors that impact on the health and development of the foetus during this period include nutrition, stress and exposure to environmental toxins. Given the importance of this phase of development, we need to rethink how best to support mothers and protect their babies during this period.
- **Infancy**. While the importance of supporting parents and infants in the first two years after birth has been recognised, and the factors that impact on health and development during this period are more widely understood, this knowledge has yet to be translated into a comprehensive and integrated approach to supporting parents and infants during this crucial period.

This review has identified a number of specific aspects of health and development which have implications for action to improve outcomes:

- **Promoting cellular health**. Our cellular health is reflected in the wellbeing of our minds, bodies and even communities. At the individual level, we can focus on stress reduction, exercise, longer sleep, healthy eating, close relationships, and exposure to nature. At the collective level we can look at improving prenatal care, protecting children from harm, reducing inequality, cleaning up environmental toxins, and improving food policies to ensure everyone has access to fresh, healthy and affordable food.
- **Promoting microbiome health**. We can overcome some of the major health challenges of the 21st century by learning how to ensure the early establishment of a healthy and diverse microbiome in infants, understanding more about the interface between the microbiome and the immune, and identifying mechanisms to re-establish a healthy complex microbiota after dysbiosis has occurred.
- **Promoting healthy nutrition**. The evidence is clear that early nutrition plays a major part in shaping children's lifelong health and wellbeing. Nutrition is one the most important and easily modifiable environmental factors in early life.
- **Promoting healthy environments**. The evidence clearly indicates that chemical exposures during pregnancy and early development are a major cause of neurodevelopmental disorders and can have a profound and lifelong impact on human health. Our efforts should be directed to trying to reduce exposures to environmental toxins in physical environments and food and consumer products by increasing public awareness and improving government and industry guidelines.

In considering how we might best address the wide range of possible interventions, we can consider four possible courses of action:

- **Let natural selection sort the problem out**. However, while human evolution is not over, the chances of natural selection adapting our species in dramatic ways to common non-infectious mismatch diseases are remote.
- **Invest more in biomedical research and treatment**. We can expect that further research will not only shed more light on the mechanisms underpinning development but also show us what we can do to prevent disturbances of development or ameliorate their effects.
- **Educate and empower**. Developing better ways of educating and empowering the general public about the evidence identified in this paper should be a priority. However, educating and empowering is not just about providing the public with more information, but is about engaging and building relationships with families at key times to help develop understandings of the evidence and how it can be applied in their context, in a way that encourages and enables families to act on the information provided. Different methods for engaging, educating and empowering families will be relevant depending on whether families are planning for a pregnancy, at risk of future unplanned pregnancies, are currently pregnant, or are currently raising a child/children.
- **Change the environment**. This involves efforts to improve the conditions under which families are raising young children. It requires strategies to address the social determinants of health and wellbeing, and reduce the social inequities that create social gradients in health and development. Central to shifting the current social gradient in health outcomes, and the social and economic burden of chronic diseases, is health equality starting in the first 1000 days. This can only be done through a coordinated policy approach which addresses the needs of children from conception, thus laying the foundation for their future health and wellbeing. As such, governments must adopt a social determinants framework across the policy and programmatic functions of all government departments and strengthen its leadership role in supporting a social determinants approach that addresses the gradient across the whole of government.

Final comment

The rapid social, economic and technological changes that have occurred over the past half century or so have been enormously beneficial in many ways. There have been dramatic improvements in longevity, standards of living, and health-care, along with reductions in violence. But, while some of these changes are for the better, some appear not to be. Our task is to understand the mechanisms that underpin development, learn how these can be disrupted by adverse experiences and exposures, and identify the environmental changes that are having these adverse effects so we can address them. This paper is a progress report on where we have got to with that task.

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