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The Interaction of Malnutrition and Neurologic Disability in Africa

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Malnutrition and neurodisability are both major public health problems in Africa. This review highlights key areas where they interact. This happens throughout life and starts with maternal malnutrition affecting fetal neurodevelopment with both immediate (eg, folate deficiency causing neural tube defects) and lifelong implications (eg, impaired cognitive function). Maternal malnutrition can also increase the risk of perinatal problems, including birth asphyxia, a major cause of neurologic damage and cerebral palsy. Macronutrient malnutrition can both cause and be caused by neurodisability. Mechanisms include decreased food intake, increased nutrient losses, and increased nutrient requirement. Specific micronutrient deficiencies can also lead to neurodisability, for example, blindness (vitamin A), intractable epilepsy (vitamin B6), and cognitive impairment (iodine and iron). Toxin ingestion (eg, from poorly processed cassava) can cause neurodisability including a peripheral polyneuropathy and a spastic paraparesis. We conclude that there is an urgent need for nutrition and disability programs to work more closely together.
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Introduction

Both malnutrition and disability are major global health problems. Over 1 billion people worldwide are malnourished¹ and 1 billion live with a disability.² Important links and interactions between both are attracting increasing

international attention with growing recognition of the potential for synergy and mutual benefit by approaching both the issues together.^{3,4}

In Africa, a recent Lancet review estimated that 56 million out of a total 158 million children (United Nations population estimates) younger than 5 years are stunted (chronically malnourished, indicated by low height for age); 6 million are severely wasted (acutely malnourished, indicated by low weight for height or low midupper arm circumference); 28 million are underweight (a combination of acute and chronic malnutrition, indicated by low weight for age).⁵ Micronutrient malnutrition is also common: 42% of children in Africa have vitamin A deficiency (serum retinol <0.70 μmol/L), 40% are iodine deficient (<100 μg/L), 24% are zinc deficient, and 20% are iron deficient (<110 g/L).⁵ Many children are affected by multiple forms of malnutrition in varying combinations and degrees.

Childhood disability is also common in resource-poor settings: 80% of the world's disabled population, of all ages, live in low-income countries, many in Africa.² Neurologic impairment is a particular problem given struggling health services and frequently suboptimal treatment of common conditions, such as perinatal asphyxia, jaundice, and infection (meningitis and cerebral malaria). Prevalence estimates

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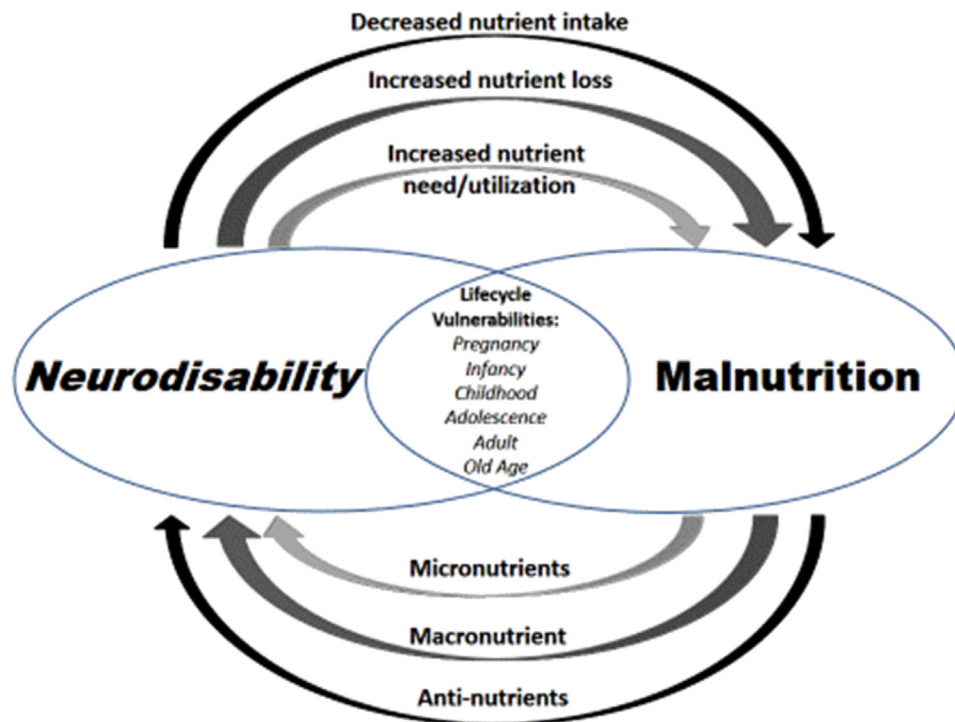


Figure 1 Neurodisability-malnutrition interactions: how neurodisability affects malnutrition and malnutrition affects neurodisability. (Color version of figure is available online.)

for childhood neurologic impairment range from 19–61 per 1000.⁶

In this review, we consider the relationship between malnutrition and neurologic disability, with a focus on Africa. Taking a life-cycle approach, we discuss how malnutrition can cause or affect neurodisability, and, in turn, how neurodisability affects nutrition (Fig. 1).

Neurodisability and Nutrition in Pregnancy and Infancy

Maternal health and nutrition are key to optimal fetal development. Risk factors for poor nutrition are common in Africa and include poverty,⁷ maternal ill health, and depression.⁸ Though humans have evolved to prioritize maternal resources toward the developing fetus/infant,⁹ maternal malnutrition can result in fetal growth restriction and low birth weight (<2500 g).⁵ Most neurodevelopment is completed during the first 1000 days after conception, that is, during intrauterine life and infancy,¹⁰ and optimizing nutrition during this period has become a global priority.^{11,12}

Maternal malnutrition can result in both global and specific neurodevelopmental sequelae. Children of underweight women are reported to have an increased risk of delayed mental development (relative risk = 1.36, 95% CI: 1.04–1.78).¹³ The hippocampus (memory), the cortex, and auditory development are particularly vulnerable to malnutrition in early pregnancy.¹⁴ Other effects of early intrauterine malnutrition only become apparent in later life,¹⁰

and include adolescent and adult problems, such as attention-deficit disorder, conduct problems, and eventual low socioeconomic status.^{15–17} Prenatal exposure to daytime fasting during Ramadan has been reported to increase the likelihood of adult disability by more than 20% in Iraq and Uganda, with substantially larger effects on mental and learning disabilities.¹⁸ Though from a very different setting and time, important warnings for African populations at risk of maternal malnutrition can be drawn from seminal studies of individuals exposed in utero to the “Dutch famine” (resulting from severe wartime food shortages during the winter of 1944–1945). A variety of neurodevelopmental sequelae included increased risk of schizophrenia, increased response to stress, and poorer cognitive performance.¹⁹ Timing of the nutritional insult is important, those exposed early in gestation being at greatest risk. Other adult disabilities are less directly linked with fetal undernutrition. Sequelae, such as coronary heart disease and diabetes,¹⁸ are key risk factors underlying stroke, a major cause of adult-onset disability.²⁰

Specific maternal nutritional deficiencies and their effects on infant neurodevelopment are shown in Table 1.

They are seldom found in isolation and it is common to have multiple deficiencies against a background of maternal undernutrition, frequent ill health, and poverty. Time-specific nutritional deficiencies during a pregnancy can alter genotype expression and induce abnormal phenotype. The developing brain between 24 and 42 weeks of gestation is particularly vulnerable to nutritional insults because of the rapid trajectory of several neurologic processes, including synapse formation and myelination. The brain’s

Table 1 Specific Maternal Nutritional Deficiencies and Their Effect on Infant Neurodevelopment

Nutrient	Source	Daily Requirement	Associated Neurodevelopmental Risk	Prevention
Folate	Dark green leafy vegetables and liver; poor biosynthesis and destroyed by over cooking	400 µg	Myelomeningocele	Preconceptual and periconceptual folic acid
Vitamin B12	Meat, eggs, milk, and cheese	0.0015 mg		Not usually necessary
Iron	Meat, poultry, fish (heme), and spinach beans (nonheme)	30-60 mg elemental iron	Cord ferritin < 76 µg/L is associated with impaired language ability, tractability, and fine motor skills at 5 y	Regular additional iron throughout pregnancy
Vitamin A	Eggs, milk, oily fish, liver, cheese, and yoghurt	0.6 mg	Anemia and auditory loss	No more than 1.5 mg/d should be taken
Vitamin D	Eggs and oily fish	0.01 mg pregnancy 7-8.5 µg baby	Low birth weight	
Iodine	Plant content depends on iodine in the soil, shell fish, and sea fish	150 µg for adult 250 µg pregnancy	Neurologic or myxoedematous hypothyroidism. Milder deficiency leads to goiter and lower IQ	Iodized salt
Zinc	Nuts, legumes, and whole grains (less available) than in dark meats	8 mg/d for adult	Autonomic and cerebellar dysfunction	No evidence of need to supplement
B 1 Thiamine	Peas, fruits, eggs, liver, and unpolished grains	0.8 mg	Intrauterine growth retardation. Auditory neuropathy spectrum disorder and language difficulty	Avoid polished grains

IQ, intelligence quotient.

Risks in pregnancy		Risks in labour	Risks to newborn
Adolescent pregnancy*	anaemia, late booking, CPD	Premature delivery	LBW, RDS, anaemia
Twin pregnancy	anaemia, abnormal lie	Premature delivery	LBW, RDS, anaemia
Short mother	CPD	LSCS or difficult delivery	HIE
Malaria in mother	anaemia	Premature delivery	LBW, anaemia
HIV + mother	anaemia, infections,	IUGR	LBW, anaemia, hypoglycaemia, FTT
Malnutrition	anaemia	Premature delivery	LBW, RDS, anaemia,

* worldwide there are 3 million teenage pregnancies/year (Save the Children)

LBW = low birth weight; RDS= respiratory distress syndrome; FTT = failure to thrive; IUGR = intrauterine growth retardation; CPD = cephalopelvic disproportion; LSCS = Caesarean section; HIE haemorrhagic ischaemia encephalopathy

Figure 2 Maternal and neonatal risk factors contributing to malnutrition and disability. (Color version of figure is available online.)

vulnerability to nutritional insults sometimes outweighs its plasticity, which explains why early nutritional insults result in brain dysfunction not only while the nutrient is in deficit in utero but also after repletion postnatally.²¹ Although all nutrients are important for neuronal cell growth and development, some are particularly so, such as iron, zinc, selenium, iodine, folate, vitamin A, choline, and long-chain polyunsaturated fatty acids.²¹ As they affect different parts of the developing brain, different long-term effects would result from varying severities and combinations of deficit.

Maternal malnutrition can also lead to neurodisability via effects on body size. A mother who was malnourished as a child may have an underdeveloped pelvis, predisposing to cephalopelvic disproportion and obstructed labor. Even with instrumental delivery and cesarean section (often delayed and frequently unavailable in resource-poor African settings), the infant is at risk of perinatal mortality and long-term morbidity.²² Illustrating the intergenerational effects of malnutrition is that women who were themselves undernourished as children tend to have underweight babies.¹⁸ Risk factors and potential interventions are shown in Figure 2 and Table 2

Neurodisability and Macronutrient Malnutrition in Children

Manifestations of macronutrient malnutrition include acute malnutrition (wasting or kwashiorkor or both), stunting and underweight.²³⁻²⁵ In some children, neurodisability may be a causal underlying factor via the following.

Decreased Food Intake

A child with cerebral palsy (CP) cannot, for example, compete for the family plate as actively as his or her siblings; cannot properly chew or swallow available family foods. A family living in poverty may make a difficult decision to prioritize healthier children who are more likely to contribute to household earnings than the child with a disability.

Increased Nutrient Loss

For example, a child with CP has frequent bouts of vomiting.

Increased Nutrient Requirement

For example, an immobile, neurodisabled child has frequent infections and sores and needs increased nutrients for adequate healing.

Alternatively macronutrient malnutrition can underlie disability, for example, malnutrition puts a child at greater risk of infection—this might include meningitis, a major cause of permanent neurologic impairment⁶; malnutrition leads to impaired cognitive development.^{26,27}

In the past, many nutritional rehabilitation programs focused on reducing the very high case fatality associated with acute malnutrition.²⁸ Severe wasting alone affects 19 million children younger than 5 years worldwide (5.5 million in Africa) but is responsible for 0.5 million deaths per year.⁵ New public, health-focused approaches to care in the community (“Community Management of Acute Malnutrition,” CMAM) are effective^{29,30} and have great potential to significantly reduce that mortality.³¹ This means that children who might previously have died will now survive

Table 2 Ways in Which to Reduce Neurologic Disorders in Infants

Preconception	During Pregnancy	At Birth	Neonatal Period
Empower girls	Provide adequate general nutrition	Skilled obstetric care	Prevent Hypoglycemia
Family planning	Provide extra daily iron and folic acid	Skilled neonatal resuscitation	Prevent hypothermia
Reduce early marriages	Treat infections	Delayed cord clamping	Chlorhexidine to cord
Folic acid supplements	Prevention of Mother To Child Transmission	Baby put to the breast	Kangaroo mother care
Iodine in salt	Bednet and malaria prophylaxis		Feed with breast milk
Vitamins A and D in flour	Give psychosocial support		
	Encourage early booking		
	Steroids if in premature labor		

and will need ongoing support. Children with underlying disability are one such vulnerable group. In a cohort of acutely malnourished children admitted to a hospital in Malawi, 7% of children had an obvious disability (mostly CP). Disability was second only to human immunodeficiency virus (HIV) as a risk factor for death.³² Although impossible to say how much of this excess mortality was avoidable and how much inevitable owing to the underlying disability, it is clear that future programs will need greater emphasis on treating and supporting (in terms of nutritional, clinical, and social needs) such children and their families.

Other opportunities for strengthening nutrition-disability interactions come with the recent “Scaling up Nutrition” (SUN) movement.¹² SUN’s focus is on tackling stunting (chronic malnutrition). Through more “inclusive nutrition” strategies, there is potential for SUN to also support children with disabilities.³ WHO/ United Nations Children’s Fund (UNICEF) Care for Child Development packages represents another key opportunity to link both the areas.³³

Finally, current treatments for macronutrient malnutrition use energy- and nutrient-dense therapeutic food pastes. These have the potential to enhance existing support programs for disabled children in whom swallowing difficulties are common.³⁴ Procedures, such as percutaneous endoscopic gastrostomy, commonly used in this patient group in resource-rich countries³⁵ are rarely available in Africa.

Neurodisability and Micronutrient Malnutrition

Micronutrients are essential for proper nutrition, often serving as cofactors in enzymatic reactions involving carbohydrate, protein, or fat catabolism. Deficiencies in both fat-soluble (vitamins A, D, E, and K) and water-soluble vitamins have neurologic consequences as does low intake or absorption of trace elements (minerals).

Vitamin A

Vitamin A is best known for its role in visual function. Mild deficiency results in poor vision in low intensity light (night blindness).³⁶ More severe deficiency leads to corneal and conjunctival damage, which can become permanent. Each year, some 250,000-500,000 children become blind from Vitamin A deficiency.³⁷

Also, vitamin A deficiency increases childhood mortality by altering immune function.³⁸ Children who are deficient have higher mortality from common childhood illnesses such as diarrhea or measles. Many countries in sub-Saharan Africa have therefore integrated vitamin A supplementation into immunization schedules.^{39,40}

B Vitamins

Patients are often deficient in more than one B vitamin, producing a mixed clinical picture. Deficiencies may occur in epidemics, most recently in Cuba where, in the mid-

1990s, approximately 50,000 people developed a progressive gait and visual disturbance from multiple B vitamin deficiencies.⁴¹ Supplementation rapidly corrected the problem. In most such epidemic deficiencies, supplementation of several B vitamins is done simultaneously, with the exceptions of vitamin B12 and folate.³⁹

Vitamin B1 (thiamine) deficiency leads to beri-beri, usually presenting as a polyneuropathy in the lower extremities. Untreated, this progresses to cardiovascular abnormalities, tremor, mental status changes, and visual disturbances.⁴²

Vitamin B3 (niacin) deficiency results in pellagra. Its main neurologic effects are neuropsychiatric abnormalities including dementia, confusion, and agitation.⁴³ The presence of diarrhea and skin abnormalities (dermatitis, skin erythema, and depigmentation) may suggest the diagnosis.⁴³

Vitamin B6 (pyridoxine) deficiency is a rare cause of intractable epilepsy. Its deficiency may also be iatrogenic, as some medications, such as isoniazid in the treatment of tuberculosis (TB), antagonize pyridoxine absorption. For this reason, isoniazid therapy should be accompanied by prophylactic supplemental vitamin-B6 throughout TB therapy.⁴⁴

Vitamin B9 (folic acid) deficiency during pregnancy increases the risk of neural tube defects in the offspring. Periconceptual maternal supplementation would prevent 50%-70% of these malformations.⁴⁵ Either individual or population-based supplementation is possible. In high-income countries, wheat flour is often supplemented with folate, dramatically decreasing population rates of neural tube defects.⁴⁶

Vitamin B12 deficiency affects both central and peripheral nervous systems.⁴⁷ Central effects include confusion, irritability, and aggression. A progressive myeloneuropathy presents with symptoms of posterior column, corticospinal, and peripheral nerve dysfunction.

Iodine

Iodine is essential for thyroid hormone synthesis, this being required for normal maturation of the central nervous system, particularly myelination. Deficiency is a preventable yet prevalent cause of impaired cognitive development: it is one of the commonest causes worldwide.⁴⁸ Impairment is most severe if the deficiency occurs early in pregnancy; miscarriage and stillbirth can also occur, as well as deafness, spasticity, and gait disorders. Milder deficiency is less obvious but no less serious in terms of population impact from lost intellectual capacity. Children whose mothers were mildly deficient can experience a mean reduction in intelligence quotient of 12-13.5 points.^{49,50}

Though salt iodization is one of the world’s great public health success stories, iodine deficiency remains a public health problem in 54 countries.⁴⁸

Iron

In Africa, poor dietary intake may be exacerbated by underlying TB, HIV, and by increased losses from parasitic infections, including malaria and intestinal helminths.⁵¹ Iron absorption and storage are complex processes: enhanced by vitamins C and A and by copper and inhibited by phytates,

calcium, and zinc.⁵² Iron deficiency leads to microcytic anemia. In mothers, this is associated with low birth weight,⁵ which is a risk factor for CP. In children and adolescents, it is associated with impaired cognition, learning, and behavior.⁵³

Treatment includes dietary supplementation and prevention and treatment of parasitic infections.⁵⁴ Large-scale supplementation is complex given evidence that iron supplementation in children without anemia may increase the risk of some infectious diseases including malaria. Therefore, targeted supplementation in children with symptomatic iron deficiency is often recommended.³⁹

Zinc

Zinc deficiency affects autonomic nervous system regulation and hippocampal and cerebellar development.²¹ There is, however, debate about its potential role at public health level, and about what difference supplementation might make.⁵⁵

Antinutrients and Toxic Nutritional Disorders

Toxin ingestion can cause neurologic damage. This often occurs at times of food scarcity when people are forced to eat unfamiliar foods, or compromise normal preparation. Cassava is a common culprit. Though it is an important food crop, proper preparation is vital because it contains toxins in its raw state. It must be washed, cut, dried in the sun, pounded, and only then cooked. If short cuts are taken, toxins may not be adequately removed.

The following are the 2 major neurologic syndromes associated with the ingestion of nutritional toxins.⁵⁶

Syndromes of Peripheral Polyneuropathy (With Prominent Sensory Loss and Ataxia)

In the 1930s, an outbreak of a clinical syndrome of visual loss, sore tongue, stomatitis, and eczema was hypothesized to be due to ingestion of cyanide-yielding bitter cassava.³⁹ Later, a syndrome of painful polyneuropathy, ataxia, and blurred vision was described.⁵⁷ Diagnostic criteria for tropical ataxic neuropathy were expanded to include myelopathy, optic atrophy, sensorineural deafness, and a peripheral neuropathy. This condition primarily affected Nigerian adults and was not uncommon. This expanded clinical spectrum syndrome is also suspected to be due to cyanide-yielding bitter cassava, a staple of the Nigerian diet,⁵⁷ though others have argued that these symptoms may be associated with other environmental factors in addition to toxic nutritional factors.⁵⁸

Syndromes of Spastic Paraparesis (With Increased Tone and Deep Tendon Reflexes But Preservation of Sensation)

Two toxic syndromes are notable, both presenting with a spastic paraparesis and intact sensation (similar to HTLV1-associated myelopathy and tropical spastic paraparesis).

Lathyrism

Lathyrism is caused by excessive ingestion of grass pea.⁵⁹ Although peas are consumed in many parts of Africa and Asia, excessive ingestion and the resulting neurologic syndrome of lathyrism is a public health problem in only 4 countries, including Ethiopia in Africa—others being India, Nepal, and Bangladesh.³⁹ Prevalence of symptomatic spastic paraparesis is approximately 14 per 10,000 population.³⁹ The condition is gradual in onset and more common in men than women, for which the reasons are unclear.

Konzo

Konzo is due to consumption of insufficiently processed bitter cassava.⁶⁰ It has an abrupt clinical onset and occurs in epidemic outbreaks. It has been reported only in Central and East Africa, specifically Cameroon, the Central African Republic, the Democratic Republic of Congo, Mozambique, and Tanzania.³⁹ A recent study of the cognitive effects of konzo demonstrated that children both with and without clinical konzo symptoms but living in an outbreak area had lower scores on standardized neuropsychological testing compared with control children from nonoutbreak areas.⁶¹ The authors hypothesized a subclinical neurocognitive form of the disease, though the confounding effect of living in an area of konzo outbreak could not be eliminated.

Infections, Malnutrition, and Neurodisability

Though described in more detail in other articles in this supplement, it is important to acknowledge the role of infection in both malnutrition and neurodisability, especially the following.

HIV Infection

HIV infection and malnutrition are intimately related. Malnutrition is a marker of advanced immunosuppression and HIV is common among malnourished children.⁶² Neurologic complications are well recognized in HIV infection. There may be multiple causes including the virus itself, opportunistic infections, or the result of antiretroviral treatment.⁶³

Malaria

Malnutrition influences both the manifestation of and susceptibility to malaria.⁶⁴ Malaria also plays an important role in childhood anemia in Africa⁶⁵—the implications of anemia have already been discussed. Malaria, like other infections affecting the central nervous system (meningitis and encephalitis being other major ones in Africa), can cause CP and other long-term neurologic disorders. These may be associated with feeding difficulties that, in turn, cause or contribute to malnutrition.

TB

An association between TB and malnutrition is well recognized, each affecting the clinical presentation, course, and mortality from the other.⁶⁶⁻⁶⁸ With malnutrition-associated, weakened immunity, there is an increased risk of latent TB developing into active disease, including TB meningitis. This can result in significant neurologic damage that, in turn, can lead to poor feeding and further malnutrition.

Conclusions and Future Directions

By describing the numerous ways in which nutrition and disability interact and interrelate, we hope that this review has made a strong case for closer links between them. This would not only support affected individuals and populations but has great potential for synergy and mutual benefit. Steps toward this are already being made: by the UNICEF Global Partnership of Children with Disabilities nutrition task force (http://www.unicef.org/disabilities/index_69132.html); in the 2013 UNICEF state of the World's Children Report (<http://www.unicef.org/sowc2013/report.html>), which focuses on children with disabilities and notes the need for more inclusive nutrition strategies; in early child development programs that benefit all children, but have particular potential to improve neurodevelopmental outcomes in the most vulnerable. It is vital that frontline health, nutrition, and disability services develop more effective and better integrated services. Progress would be greatly helped by

- Better data and documentation on both conditions and their interrelationship: to drive better policy, resource allocation, and evaluation of program effectiveness. Capturing comorbidity is especially important as multiple problems contribute to poor outcomes. It is vital to capture—and then address—factors that exacerbate vulnerability, such as gender, poverty, and other modifiable socially mediated risks.
- A life-course approach in which it is recognized that many later-life and adult conditions that have their origins in childhood would enable more effective programming and more rational allocation of effort and resources. This needs to balance the need to care for affected individuals while at the same time working to reduce the incidence of future problems.
- Greater emphasis must be placed on multidisciplinary approaches to both prevention and treatment services. This requires better interdisciplinary dialog and cooperation—which can only be of benefit to the increasing numbers of individuals at risk of or affected by more than one health problem.

We end on a positive note: much of the “disease burden” of malnutrition and disability results from the fact that vulnerable children who previously would have died are now surviving into later childhood and even into adulthood.⁶⁹ This mortality reduction is clearly welcome but

brings with it the need and a responsibility to provide the best possible care and opportunities for all. Far from being a problem, this should be seen as a great opportunity for better future health and social services.

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