

Born Preterm: A Public Health Issue

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Keywords

Morbidity · Premature birth · Prematurity · Public health · Very low birth weight

Abstract

Background: Prematurity accounts for about 10.6% of neonates worldwide and tends to increase as does survival from lower gestational ages. **Summary:** The importance of preterm birth in public health stems from its link to infant and under-5 mortality, morbidity, and its economic impact. In both the short and long term, preterm birth consequences are inversely related with gestational age and carry a higher risk of mortality and morbidity with neurodevelopmental, sensorial, cognitive and physical health disturbances. Individuals needing life-long support pose challenges to the responsiveness of health services and community systems. Public health can be decisive in prematurity prevention, providing data to policy-makers and reducing modifiable risk factors. This paper focuses on the long-term consequences of preterm birth and possible public health measures to tackle them. **Key Messages:** Addressing social determinants of health can have the highest impact on prematurity outcomes.

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Nascer pré-termo: Um problema de Saúde Pública

Palavras Chave

Morbilidade · Muito baixo peso · Nascimento pré-termo · Prematuridade · Saúde pública

Resumo

Introdução: A nível mundial a prevalência da prematuridade (10.6%) é crescente bem como a sobrevivência em idades gestacionais menores. **Sumário:** A importância da prematuridade prende-se com o contributo para a mortalidade infantil, para a inferior aos 5 anos e para a morbilidade, com impacto económico. A curto e longo prazo, as consequências do nascimento pré-termo relacionam-se inversamente com a idade gestacional, comportam maior risco de alterações neurológicas, sensoriais, cognitivas, comportamentais e na saúde geral. A necessidade de apoio pode prolongar-se ao longo da vida, põe à prova os serviços de saúde e comunitários. A Saúde Pública pode ser decisiva na prevenção da prematuridade, fornecendo aos decisores dados que permitam a redução de riscos modificáveis. Os autores focam-se nas consequên-

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cias a longo prazo e na abordagem da prematuridade no âmbito da Saúde Pública. **Mensagens chave:** A intervenção nos Determinantes Sociais de Saúde poderá ter impacto decisivo no prognóstico da prematuridade.

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Introduction

Preterm birth (PB) is defined as birth occurring before 37 weeks or 259 days of gestational age (GA) [1]. Prematurity is the main cause of an estimated one million neonatal deaths globally every year and a significant contributing factor to morbidities extending to adulthood [2, 3]. PB is sub-classified according to GA at birth into extremely preterm (<28 weeks), very preterm (28 to <32 weeks), and moderate to late preterm (32 to <37 weeks) [4].

The risk of PB is considerable for both the higher and lower-income countries. However, there is a dramatic difference in survival of premature babies depending on where they are born. In high-income countries, half of the babies born at 24 weeks survive, while in low-income countries, half of those born at 32 weeks still die due to a lack of essential newborn (NB) care [5]. In developing countries, the higher PB rate is commonly associated with infection (malaria, HIV) and malnutrition [6]. In most affluent countries, the improvement of socioeconomic conditions, technological development, reproductive medicine's success, and high quality of perinatal care contributed to a heterogeneous prematurity rate but also to an increased survival of extreme premature infants and a decreasing viability threshold [7–10].

Survival to PB led to the emergence of a population of complex patients with different comorbidities, whose severity and frequency are inversely associated with GA [11–17]. Some of the classic pathologies related to prematurity have diminished significantly in the last decades: hyaline membrane disease, bronchopulmonary dysplasia, necrotizing enterocolitis (NEC), and retinopathy of prematurity (ROP). Yet, neurological morbidity, more specifically intraperiventricular hemorrhage (IPVH), presented no parallel decrease [4, 12, 14, 18, 19].

Low birth weight (LBW) is defined as the weight less than 2,500 g, very low birth weight (VLBW) less than 1,500 g, and extreme low birth weight (ELBW) less than 1,000 g [1]. LBW can occur as a result of restricted fetal growth or PB. LBW infants have a greater risk of poor outcome [20]; however, GA is a better predictor of mortality and morbidity than birthweight [21–23].

Children born prematurely, especially those of extreme PB, have an increased risk of lifelong effects on neurodevelopment with motor, cognitive, sensorial, physical, behavioral and psychopathological disturbances, compared with their term peers [24–26]. They require differentiated clinical care, early intervention, special educational programs, and social interventions, which burden families and health and community support systems [8, 27–31].

PB is a public health (PH) issue due to its worldwide prevalence, increasing survival rate, short and long-term morbidity, high economic burden, and because it contributes to infant and under-5 mortality rates. This wide-ranging impact has demanded attention in many high-income countries [15, 19, 29, 32–35].

The enlarged concept of “people born preterm” can help healthcare providers to understand their long-lasting needs, provide access to health resources available to support postnatal infant development, and improve awareness of atypical clinical profiles in the long-run [36]. This review addresses PB as a PH matter focusing on its life-long consequences and strategies to tackle them.

Prematurity: Prevalence

According to Chawanpaiboon et al. [37], the global estimated preterm rate is increasing, ranging from 9.8% in 2000 to 10.6% in 2014. The estimated regional PB rates ranged from 13.4% in North Africa to 8.7% in Europe. Even though 81% of these PB occurred in Asia and Sub-Saharan Africa, data from some high-income and high-middle-income countries suggest that their PB rates are also increasing [37, 38]. According to data available from 67 countries, prevalence was higher in moderate or late preterm (84.7%), followed by very preterm (11.3%) and extremely preterm infants (4.1%) [4, 37]. However, there are some challenges to the global interpretation of preterm epidemiology that can interfere with PB rate estimation: diverse assessment methods of GA, prematurity definitions, data availability, and varying quality of vital statistics between countries [4, 37, 39].

The 2015 European Perinatal Health Report [38] pointed out that prematurity rates are heterogeneous but may be increasing in most European countries when comparing 2010 with 2015, where they range between 6 and 12% of live births [20, 38, 40, 41] (Fig. 1). The reasons for these trends are not always understood. A range of factors have been put forward: GA assessment criteria, multiple preg-

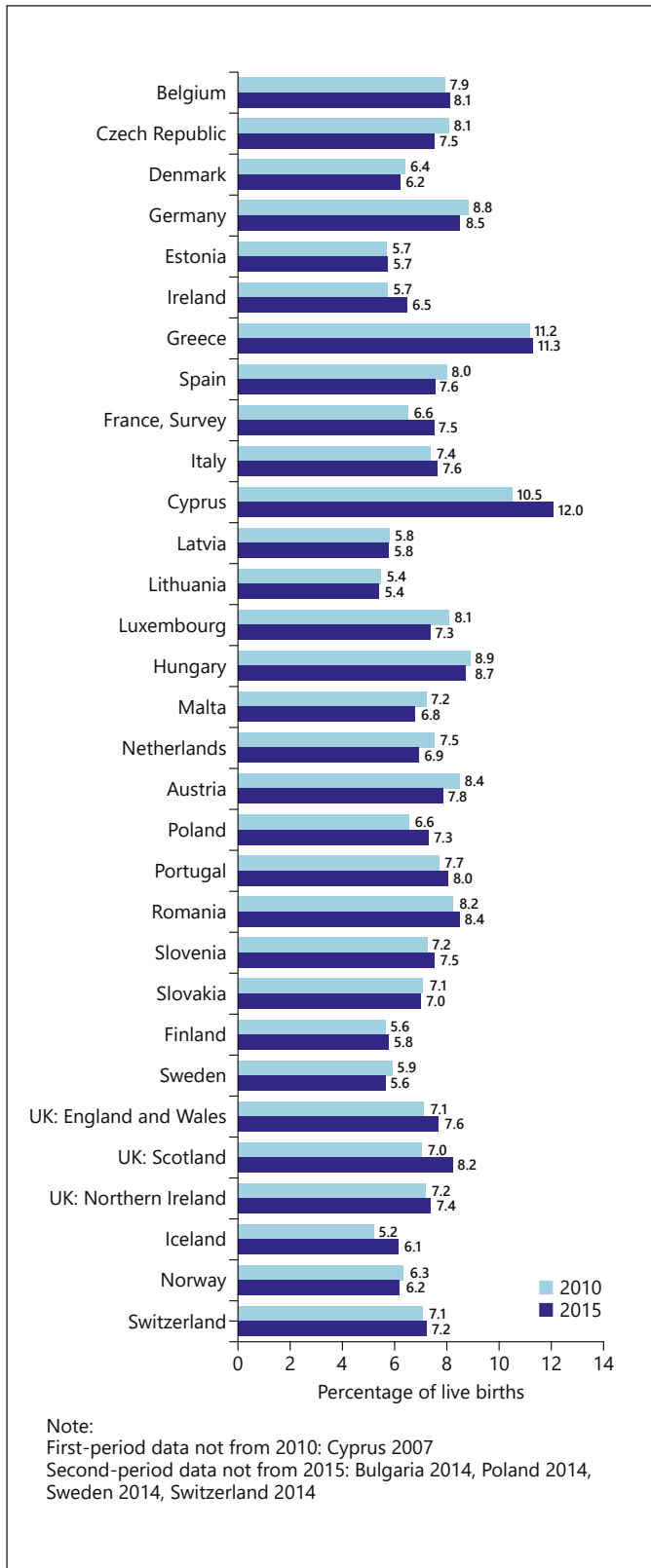


Fig. 1. Percentage of preterm live births in Europe in 2010 and 2015. Source: Euro-Peristat Project [38].

nancy rates, late maternal age, extreme body mass indexes, and socioeconomic issues, with lower-income families being at higher risk [4, 32, 34, 38, 41]. Some high- and middle-income countries have increased numbers of provider-initiated PBs [20, 42]. Probably, higher survival has changed the perception of risks associated with prematurity, which led to an increase in non-spontaneous births [41].

It is estimated that 15–20% of all births worldwide are LBW. In almost all OECD countries, the proportion of LBW infants has increased over the past two decades, being 6.5% in 2015, representing a rise of 15% between 1990 and 2015, mainly due to increase in PBs. [20] (Fig. 1)

In Portugal, prematurity has remained relatively stable in the second decade of the 21st century. According to Statistics Portugal (INE), the prematurity rate was of 7.8% in 2012 and 2013, 7.7% in 2014, 8% in 2015, and 7.8% in 2016 [20, 43]. According to 2017 OECD indicators of health outcomes, Portugal registered an increase of 59% of LBW infants since 1990 [20].

Prematurity: Risk Factors

Prematurity can be the result of a complex combination of medical, biological, genetic, psychosocial, and environmental conditions [44]. However, in about two-thirds of the cases the cause remains unknown, while the other third occurs upon medical recommendation for a wide-range of maternal and fetal pathologies [42, 45, 46].

Amongst multiple maternal risk factors, the following are emphasized: previous preterm deliveries, pregnancy at youngest or latest ages, short intervals between pregnancies, nutrition, lifestyle (physical activity, stress, workload), individual behavior (alcohol, tobacco, illicit drugs), social issues (unemployment, social support, relationship status, personal resources), medical maternal and pregnancy conditions (chronic hypertension, hypertensive disorders of pregnancy, diabetes mellitus, cardiac, respiratory, renal, autoimmune diseases, hyperthyroidism, infection), and infertility treatments [5, 6, 47].

Better understanding of the causes of PB will advance the development of solutions to prevent it [46].

Prematurity: Impact on PH

Mortality

Globally, circa 44% of deaths in children under under-five occurred in the neonatal period, PB being the commonest cause of neonatal death [20, 48, 49]. Approxi-

mately 1 million children die each year due to complications of PB [2, 20].

Each additional week of gestation results in an increased survival rate [29, 49]. The GA survival threshold, defined as long-term survival above 50% [50], has been decreasing. In some high-income countries, it is as low as 23 weeks [49]. Survival without major morbidity in VLBW infants is increasing, ranging from 53 to 71% in different studies [49, 51, 52].

The overall in-hospital survival differs among neonatal networks from 78 to 93% – range at 24 weeks 35–84% and at 29 weeks 92–98% [53]. Stoll et al. [12] described survival at discharge of 6% at 22 weeks and 92% at 28 weeks. In a study from Canada, Johnston et al. [138] estimated similar survival rates amongst live births at age 2 and 10, circa 56.0% survival at <28 weeks, 92% at 28–32 weeks, and 98% at 33–36 weeks. Cheong et al. [54] describe a 73% survival at 8 years of a corrected age in a cohort of extreme preterm [11, 12].

In a Swedish population-based study, Crump et al. [25] described that, among individuals born in the 1973–1979 period, low GA at birth was independently associated with increased mortality in young adulthood.

The survival threshold in Portugal is 25 weeks. According to the Portuguese Very Low Birth Weight Infant Registry, in 2013, the overall survival rate was 89%. Per GA intervals, survival rates were 95.3% for 28 and 31 weeks, 77.6% for 25 to 27 weeks, and 42.1 and 16.7% for 24 and 23 weeks, respectively [55].

Reducing mortality associated with complications of prematurity will be crucial to reduce worldwide under-five mortality.

Morbidity

Improved survival of preterm infants leads to short- and long-term higher risk of neurological, cognitive, sensorial, respiratory, digestive, renal, cardiovascular, metabolic, immune, and psychosocial disturbances [4, 22, 25, 26, 36, 56, 57]. We will focus preferentially on those morbidities that are life-long in extreme and very preterm infants.

Neurodevelopmental impairment (NDI) is displayed in 5% of all PBs [58]. Survival without NDI at 2 years of age has become a common benchmark for success. While most neurodevelopmental disabilities are not major deficits, they should be clinically considered [59]. Some of these morbidities are not evident at discharge or even at 2 years of age [59]. Therefore, long-term follow-up is needed to properly evaluate the consequences of PB.

In the early years of life, preterm infants often continue to experience physical health problems that may re-

quire frequent medical visits and re-hospitalization. This may limit their participation in regular childhood activities, which may in turn affect their social skills.

Neurological morbidity is responsible for a high risk of cognitive, motor, and sensory impairment. Periventricular leukomalacia (PVL), IPVH, and post-hemorrhagic hydrocephaly are the main determinants of neurodevelopmental outcomes [17, 22, 60–65]. Motor deficits in children born preterm are generally identified earlier, but some of them are transitory (poor head control, hypotonia, or hypertonia) disappearing near 12 months [66]. However, some psychomotor disturbances will initially be clinically silent [67]. Different studies among VLBW/ELBW children at school-age [68] and ELBW children at ages 11–13 years [61] found a higher likelihood for developmental coordination disorder and an increased risk for long-term motor impairment. Preterm infants surviving into adulthood after neonatal IPVH or PVL continue to be at very high risk of poor neurological outcomes [69].

Cerebral palsy (CP) is one of the major neurological complications of premature birth. Survivors of extreme prematurity have rates of CP in childhood 70–80 times higher than those in term infants [17, 70–73]. Studies of time trends in the prevalence of CP have shown different results [37, 70, 73–75]. For children born in Portugal in 2001–2007, the prevalence of CP at 5 years of age was estimated to be 4.6-fold higher in children born at 32–36 weeks' gestation, 45.1-fold higher in those born at 28–31 weeks, and 70.1-fold higher in children born at <28 weeks' gestation, compared with children born at term (Table 1) [76].

Diagnosis of high CP risk can be established by 6 months of corrected age with a combination of medical history, standardized motor assessment and neuroimaging [15, 17]. Most studies of VLBW infants show cognitive deficits (lower intelligence quotient, intellectual, learning disabilities, and executive dysfunction), academic underachievement and grade failures [77]. Early referral to CP-specific early intervention is critical to improve functional outcomes.

ROP is the main cause of visual deficit in preterm infants [78]. They have an increased risk of long-term visual disorders due to the combination of development interruption of the visual system due to preterm delivery and/or neurological complications, oxygen toxicity, infection, glycemia disorders, undernutrition, and genetic factors [15, 77–82]. ROP is a progressive disease characterized by fibrovascular proliferation at the periphery of the retina with risk of retinal detachment. It has a multifactorial etiology, prematurity being its main

Table 1. Cerebral palsy risk at 5 years of age associated with gestational age at birth

	<28 weeks	28–31 weeks	32–36 weeks	>36 weeks
Live births	1.937	4.803	46.774	711.525
Registered cases	109	174	174	571
Incidence rate	56.27	36.23	3.72	0.80
Incidence rate, 95% CI	46.86–6.44	31.30–41.89	3.21–4.31	0.74–0.87
CP risk <28 vs. >36 weeks	Relative risk 70.12; 95% CI 57.41–85.64			
CP risk 28–31 vs. >36 weeks	Relative risk 45.14; 95% CI 38.19–53.57			
CP risk 32–36 vs. >36 weeks	Relative risk 4.64; 95% CI 3.91–5.49			

CP, cerebral palsy; CI, confidence interval. Children born in Portugal between 2001 and 2007 ($n = 1,098$). The lower risk group (<36 weeks of gestational age) is considered the reference group to cerebral palsy relative risk calculation at 5 years of age. Data from October 31, 2016. Reproduced with permission from reference [76].

determinant [83–85]. It is recorded in about 2–11% of VLBW infants [77, 83]. The rate of blindness and/or severe visual impairment is inversely related to GA (1–2% at 26–27 weeks and 4–8% at ≤ 25 weeks) [77]. Myopia and hypermetropia arise in at least a quarter of children born <28 weeks [86]. The need to prescribe glasses is also related to GA, with 24% at the age of 6 <26 weeks' GA wearing glasses versus 4% of term controls. This difference continues into adolescence and adulthood [87, 88]. A high rate (4–5%) of late retinal detachment in ELBW infants during their late teens has been observed [79, 81, 88].

Hearing impairment has a detrimental effect on the development of language, learning, communication skills, quality of life, and on economic independence in adult life [89, 90]. VLBW infants have central auditory processing difficulties, including in discerning simple speech sounds and worse auditory recognition than their full-term counterparts [91]; a prevalence of 0.1–0.2% has been reported [92], and may be 10–50% higher in VLBW infants [77, 87, 92]. Hypoxia, hyperbilirubinemia, infections, ototoxic therapeutics, and exposure to noise can irreversibly damage the cochlear, vestibular organs, the auditory nerve, and cortex [92]. Hearing loss may be progressive and diagnosed late in life (2–4 years of age), requiring long-term surveillance to timely introduce hearing aid wear [92, 93].

Cognitive deficit is the most prevalent disability in the population of preterm children. Very preterm survivors have high rates of cognitive dysfunction and emotional troubles at school age that affect academic functioning and progress [94]. Case-control studies have shown that very preterm children have significantly lower intelligence quotient scores than term peers. The most signifi-

cant neonatal risk factors are severe IVH, PVL, neonatal seizures, NEC, and long-term ventilation [95]. Cognitive dysfunctions seem influenced by environmental factors such as parental socioeconomic status and education [95, 96]. Follow-up revealed that many of the difficulties persisted into adolescence and early adulthood [94]. Long-term monitoring will be important to identify later cognitive impairment and educational needs.

Language disorders have been reported in children born preterm in its different domains (receptive, expressive, articulation). Several biologic and environmental factors influence language outcomes. Regular exposure to speech is essential to auditory cortex and speech development, social interaction and later school achievement [97, 98].

Behavioral and psychopathological disturbances are more prevalent in individuals born preterm and are also inversely related to the GA. These disturbances often coexist with motor, language, and cognitive problems [51, 99–102].

The risk of behavioral problems, such as attention deficit hyperactivity disorder, is increased by 2.6–4 times in very preterm infants in early childhood. They also often present more school problems and anxious and depressive symptoms, risk of hospitalization for mental disorders and borderline behavioral problems while transitioning to adolescence. However, they were less prone to delinquency and risk-seeking behaviors than control young adults [16, 99, 103]. Lower self-esteem, lower employability, and lower income have also been reported as frequently found in adulthood [104, 105]. Nevertheless, the self-perception of the quality of life seems to be positive [16]. The relevance of the screening for behavioral and psychiatric changes and timely intervention in this area is emphasized.

Bronchopulmonary dysplasia is defined by oxygen dependence after 28 days of life or 36 weeks of postmenstrual age [106]. Arrested vascularization and augmented vasoreactivity may lead to the development of pulmonary hypertension in the weeks and months after PB [107–109]. It has a prevalence of about 40% in infants born at GA <28 weeks [110]. It is associated with invasive ventilation, oxygen toxicity, pre- and postnatal infection, nutritional deficit, and possible genetic susceptibility [106, 111]. In the long term, respiratory impairment, particularly if exposed to noxious substances, has been observed resulting in changes in the respiratory function, bronchial hyperreactivity, sometimes with an atypical clinical profile (asthma-like), reduced tolerance to exercise, increased risk of respiratory infections needing hospital admission, pulmonary hypertension, some needing ventilation support at home [19, 30, 106, 112].

Intestinal failure is a reduction in the functional gut mass below a critical threshold necessary to maintain growth, hydration, and electrolyte balance [113]. The leading cause of intestinal failure in neonates is anatomic short bowel syndrome, and NEC inflammation and necrosis of the intestinal wall are its predominant cause in VLBW infants [102, 113–115]. The long-term need for parenteral nutrition is associated with cholestasis, hepatic insufficiency, long-term central catheters, and higher risk of infections [15, 116]. Besides a high lethality (15–60%), advances in parenteral nutrition, infection prevention, surgery techniques, and transplantation have improved prognosis [117].

High-risk renal long-term outcomes in preterm NB appear to be associated with early acute renal injury [115, 118]. PB occurs in the active phase of nephrogenesis, resulting in fewer nephrons. Nephrotoxic medications can potentiate kidney function impairment, increasing the risk of chronic kidney disease [119, 120]. Acute neonatal kidney injury risk is around 12–39%, even though its connection with chronic kidney disease is not yet clear [118]. These patients should be monitored regularly for long-term kidney damage [121, 122].

Cardiometabolic syndrome (CMS) is a combination of metabolic dysfunctions characterized by resistance to insulin, diminished tolerance to glucose, dyslipidemia, hypertension, and intra-abdominal adiposity [123]. Barker et al. [124, 125] suggested, in the late 1990s, the inverse correlation between LBW, risk of cardiovascular disease, and type 2 diabetes in adult life. Variations in fetal and postnatal nutrition could be linked to the modification of genetic expression, resulting in the programming of long-term chronic disease [126, 127]. In the long run, CMS is

also reinforced by lifestyle: less physical exercise and inadequate diet. Adequate interventions may reduce the impact of this pathology [126, 128].

Venous thromboembolism (VTE) is considered to be a complex disorder influenced by several genetic and environmental factors and affects circa 1 in 1,000 individuals per year [129]. Zöller et al. [130], found that low GA at birth was associated with an increased risk of VTE in infancy, early childhood, and young adulthood, suggesting that PB could be an important risk factor for later VTE [129, 131].

Disorders of the immune system can account for the high susceptibility of preterm neonates to infection [132–135]. PB interrupts the fetal acquisition of passive immunity and favors a different, precocious dermal and gastrointestinal microbiome acquisition, different from that of term neonates [132–137]. Better understanding of the characteristics of the immune system in preterm infants is challenging [135].

Economic Impact

The economic impact of prematurity is assumed to be high, including not only the immediate neonatal intensive care costs but also ongoing long-term complex healthcare needs. The complexity of the clinical situation of some survivors, particularly those of earlier GA, determines the need for concerted multidisciplinary action and a consequent response by health, social, community, rehabilitation and special education departments.

The US Institute of Medicine (IOM) published in 2007 the report “Preterm Birth, Causes, Consequences and Prevention”, in which the estimated economic impact (medical, educational and lost productivity combined) of PB in the USA in 2005 accounted for USD 26.2 billion or USD 51,600 for each child born prematurely [44]. The average first-year medical costs, including both inpatient and outpatient care, were about 10 times greater for preterm (USD 32,325) than for term infants (USD 3,325). The average length of stay was nine times longer for a preterm NB (13 days), compared with a baby born at term (1.5 days) [44].

Johnston et al. [138] concluded in 2014, that PB resulted in significant morbidity, mortality, and high costs for health services in Canada. Although the highest expenditure was concentrated in the neonatal period, the costs and resources use continued throughout childhood. Whilst the largest group was composed of moderately premature infants, it was the group of extreme prematurity that cost the most [138].

A systematic review by Petrou et al. [139] on the long-term costs of prematurity after hospital discharge concluded that PB and LBW result in substantial costs for health systems, special education, social services, family and caregivers, and society in general.

Blencowe et al. [56] estimated that in 2010 all PBs worldwide would have been responsible for 77 million disability-adjusted life years, accounting for 3.1% of the global total, of which 3 million would be years lived with disability.

The evaluation of direct healthcare costs associated with prematurity encompasses both hospital admissions (initial and subsequent) and those related to outpatients (therapies, clinical, educational, and social support). Out-of-pocket expenses were substantial and significantly higher for very preterm and VLBW infants [5]. The indirect costs (loss of productivity of the caregivers, emotional stress, and repercussion on the families and quality of life) although more difficult to assess, should be considered to allow for a more comprehensive quantification of the burden of individuals surviving prematurity. Several authors have drawn attention to the high social costs from a family perspective [28, 140, 141].

MPT Infants

Babies born MPT account for more than 80% of all PB, of which the majority remained without disabilities in the long-term; however, when compared to full-term infants, they have increased mortality and experience higher morbidity, which had been underestimated in the past [138].

Johnston et al. [138] describe a survival rate of 93% at age 2 and 10 in moderate, and 98% in late preterm infants; the majority of children remained disability-free at age 10.

MPT however, have higher rates of mortality and short-term morbidity. Worse neurodevelopmental and school performance outcomes, increased risk of CP and costs per infant than their term peers, have been pointed out [138]. Other common neonatal morbidities in these infants include hypothermia (known to be associated with worse outcomes), hypoglycemia (increasing likelihood of long-term neurological sequelae), difficulties in establishing oral feeding (slow feeding, choking episodes, desaturation events, bradycardia, and apnea), jaundice, and short and long-term respiratory compromise (respiratory distress syndrome, transient tachypnoea and pneumonia, increased risk of bronchiolitis and wheezing) [142–144].

Long-term health and neurodevelopmental problems, as well as educational difficulties are known to occur [25].

Although very and extreme preterm infants were associated with the highest expenditures, MPT healthcare needs impact significantly upon pediatric healthcare, due to their larger population size [138, 143].

Prematurity: Prevention

PH can be decisive in reducing modifiable risk factors of prematurity, improving perinatal care, and supporting postnatal infant development. Whilst the risk of adverse outcome is highest among very preterm [18, 96], MPT represent a large population for whom PH policy can be most effective [103, 143–145].

The prevention of prematurity requires a multifaceted approach aiming to globally improve women's health, starting before pregnancy but also focusing on preconception and gestational periods [44, 146]. Intervention on social determinants of health can reduce some risk factors, influencing PB rates and outcomes [147]. PH intervention can be crucial in controlling adverse social conditions, namely poverty, discrimination, violence, low education, and intervention for behavioral factors (alcohol, tobacco, or illicit drug use); regulations to protect women from workload or exposure to potential harmful pollutants, improving adequate spacing (>24 months) and preventing teenage or unintended pregnancies [44, 147].

In the preconception period, equality in access to primary, preventive, and obstetric risk care is highlighted. Regimentation of assisted reproductive therapies (ART), aimed to reduce the risk of higher-order multiples, focused on reducing the number of embryos for transfer (elective single embryo transfer policy) and eventually limiting candidate's age to ART, are relevant issues [148, 149]. During gestation, the relevance of early identification of women at risk for preterm delivery has been stressed as it leads to effective preventive treatments, control of chronic diseases, optimization of body mass index, eradication of non-medically indicated deliveries before 39 weeks, and effective management of preterm labor [5, 44].

In assessing adequate preterm delivery, occurring in a high-level quality care, neonatal resuscitation, comprehensive neonatal intensive care, special infant feeding support, and management of neonatal complications are important issues.

It is essential to put in place adequate policies to integrate premature babies within interventional programs to track long-term disabling outcomes and to support postnatal infant development [150].

The need to research prematurity causes and their interrelationship, to search for newer therapeutics and preventive approaches of PB is key. PH can provide population-based surveillance systems to monitor trends in prematurity, prevention efforts, risk factor evolution, and outcomes in PB [151–153].

Conclusion

The increasing survival at progressively lower GA with a higher risk of morbidity, draws attention to the high number of people surviving from prematurity in terms of PH [28, 41, 154]. Dissemination of knowledge about the causes and prevention of PB, the extent of morbidity and mortality associated to prematurity, and

their impact on families and support structures must be relevant to policy makers. Addressing social determinants of health can reduce PB rates and improve outcomes. This knowledge and consequent multifaceted action may contribute to gains in terms of health economics and optimization of the human potential of individuals born preterm and their families. The burden of PB highlights the crucial importance of prematurity prevention – it must be a priority issue in health policy makers' agenda.

Disclosure Statement

The authors have no conflicts of interest to declare.

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