

The health consequences of low birth weight: literature review and critique

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1. Introduction

This paper reviews the literature on the child health consequences of low birth weight (<2,500g) in Europe.¹ Its focus is on how these consequences are mediated by the social environment of the child at birth and in early childhood.

1.1. The increasing incidence of low birth weight

In almost all developed countries, the proportion of low birth weight has increased over the past two decades. In the US, it increased from 6.8 percent in 1980 to 7.4 percent in 1998. In Japan, the increase over the same period was somewhat more dramatic, from 5.2 percent to 8.1 percent (Table 1). With a few exceptions (e.g. Hungary - see Gourbin and Gardos, 2003), proportions have been increasing in Europe too: in Finland from 3.9 percent in 1980 to 4.4 percent in 1998; in Sweden from 4.1 percent to 4.4 percent over the same period; in Austria from 5.7 percent to 6.1 percent; in Greece from 5.9 percent to 7.4 percent; and in Bulgaria from 6.1 percent to 9 percent.

In relative terms, the increase in the proportion of very low birth weight has been larger. Table 2 shows that in Belgium, for instance, the proportion of low birth weight increased from 5.5 percent in 1980 to 6.1 percent in 1990, while that of very low birth weight increased from 0.54 percent in 1980 to 0.70 percent in 1990 (and 0.73 percent in 1994 - Masuy-Stroobant et alii, 2000, calculated based on pp. 22-23).

¹ Low birth weight is usually defined as birth weight below 2,500g, very low birth weight as birth weight below 1,500g, and extremely low birth weight as birth weight below 1,000g (WHO). For a brief critical discussion of this definition, as well as for a brief discussion of the difference between low birth weight and premature birth see Appendix 1.

Table 1: Proportion of low birth weight in Europe, the US and Japan 1970-2002

Year	1970	1975	1980	1985	1990	1995	1998	2000	2002
EU-15 countries									
Austria	-	-	5,7	5,8	5,6	5,7	6,1	6,3	6,6
Belgium	-	-	-	-	6,1	6,8	-	-	-
Denmark	-	-	-	4,9	4,2	5,5	4,9	4,9	5,3*
Finland	-	5,5	3,9	4,1	3,9	4,3	4,4	4,6	4,5
France	-	-	-	-	-	5,7	6,7	-	-
Germany	-	-	-	-	-	6,1	6,4	-	-
Greece	-	-	5,9	6	6	6,8	7,4	8,1	-
Ireland	-	-	-	4,1	4,2	5,3	5,6	-	-
Italy	-	-	-	-	5,6	-	5,9	-	-
Luxembourg	-	-	-	4,9	4,3	4,1	3,8	7,5	-
Netherlands	-	-	-	-	-	-	-	-	-
Portugal	-	5,9	4,6	5,3	5,6	6,0	6,7	7,1	7,4
Spain	-	-	-	4,5	5	5,8	-	-	-
Sweden	4,3	4,7	4,1	4,6	4,5	4,4	4,4	-	-
UK & Northern Ireland	-	-	-	6,9	6,7	7,2	-	-	-
EU-15 average	-	-	-	5,7	5,7	6,2	6,3	6,5	6,3

Central & South Eastern Europe									
Albania	-	-	-	-	7	9,3	5,7	4,8	4,6
Bulgaria	-	-	6,1	6,1	-	8	9,0	8,9	8,8
Croatia	-	-	-	-	-	5,9	5,4	6,5	5,6
Czech Republic	6,2	6,2	5,9	5,6	5,5	5,5	5,9	5,8	6,2
Estonia	-	-	-	-	-	4,4	4,5	4,3	4,6
Hungary	-	-	10,2	-	9,3	8,2	8,3	8,4	8,5
Latvia	-	-	-	4,6	4,5	4,8	5,2	5,4	5,4
Lithuania	-	-	-	-	3,7	4,2	4,5	4,6	4,9
Poland	-	-	-	7,8	-	6,68	6,2	5,72	5,9*
Romania	-	-	-	7,1	7,2	9,0	9,0	8,9	8,8*
Slovakia	-	-	6,2	6	6	6,9	6,5	6,7	7,1
Slovenia	-	-	-	5,5	-	5,1	5,7	5,8	6,0
FYR. Macedonia	-	-	-	3,8	8,6	11,1	6,6	19,2	16,0*
Others									
US	7,9	7,4	6,8	6,8	7	7,2	7,4	-	-
Japan	5,7		5,2	5,7	6,3		8,1	-	-

Source: Europe: World Health Organization European 'Health for All' database (<http://hfadb.who.dk/hfa/>)

US and Japan: World Bank HNP stats (Health, Nutrition and Population) (<http://devdata.worldbank.org/hnpstats>) part of WDI (World Development Indicators)

Note 1: WHO is based on “% of live births weighing 2500g or more – both sexes” and World Bank is based on “Low birth babies – (% of births)”.

Note 2: Figures for Denmark, Poland, Romania, and FYR. Macedonia (marked *) in 2002 is data for 2001.

Table 2: Very low birth weight (<1500g) and low birth weight (<2500g) births. Selected European countries 1970-90, Incidence per 1000 live births

Country	1975		1980		1985		1990	
	<1500g	<2500g	<1500g	<2500g	<1500g	<2500g	<1500g	<2500g
Austria		-		-	8.25	57.84	7.70	55.97
Belgium		-	5.44	54.82	7.10	58.90	6.99	60.82 ^a
Czechoslovakia (ex)		62.96	7.60	59.29	6.62	56.93	7.11	55.95
England & Wales		-	7.80	65.29 ^b	9.00	68.13	9.82	67.47 ^c
GFR (ex)		-		55.14		57.31		57.62 ^c
Hungary	17.41	111.76	15.33	103.54	15.07	99.38	12.94	92.73
Italy	8.44 ^d	67.41 ^e	5.73	51.41	6.38	52.30		-
Poland ^f	8.45 (12.51) ^g	72.78 (76.83)	8.53 (12.80)	75.79 (80.07)	9.01 (12.73)	77.80 (81.52)	9.82 (13.30)	80.53 (84.02)
Portugal			4.81	48.48	5.77	53.99	6.36	56.36
Switzerland			5.27	51.32 ^h	5.78	50.82 ⁱ	6.57	51.27

Source (direct): Masuy-Stroobant and Gourbin, 1995, p. 73

Note: a. 1988; b. 1981; c. 1989; d. <1550g (1973); e. <2550g (1970); f. <1501g and <2501g; g. (in brackets) including the “non viable births with signs of life”; h. 1979-81; i. 1986

In England and Wales, the incidence of low birth weight increased from 6.5 percent in 1980 to 6.7 percent in 1990, while that of very low birth weight increased from 0.78 in 1980 to 0.98 percent in 1990 (and 1.2 percent in 1996 - Masuy-Stroobant and Gourbin, 1995, p. 73; Petrou, 2003, referring to Macfarlane and Mugford, 2000).

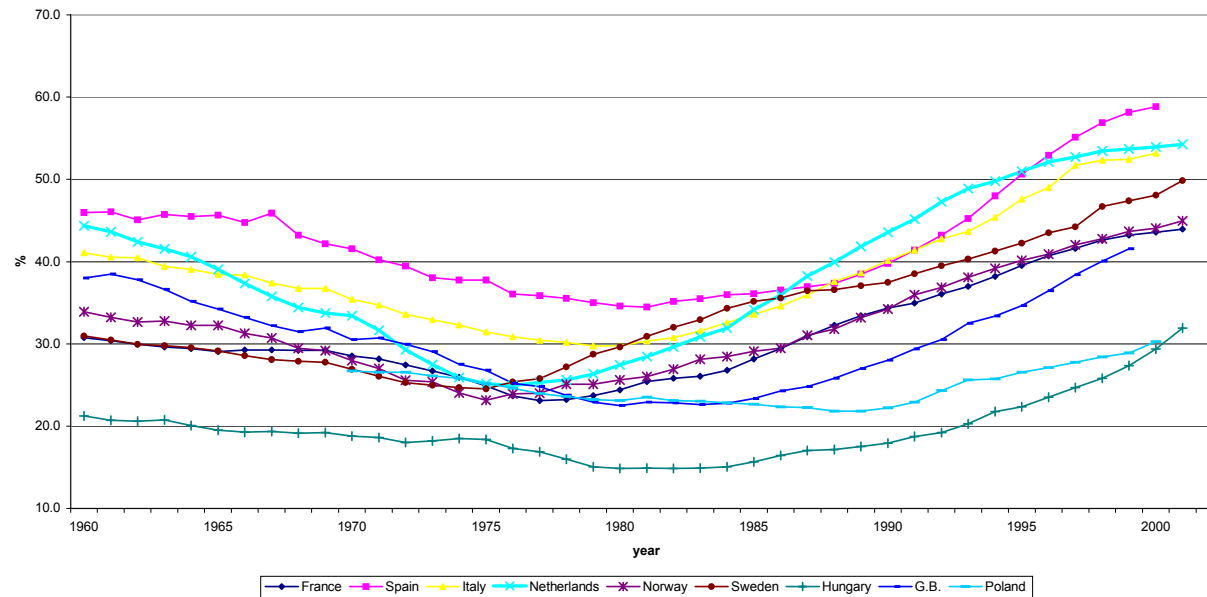
These increases should be put in perspective, however. The incidence of low birth weight is still low everywhere and even lower in the EU-15 than in either the United States or Japan. Table 1 shows that in 1998 low birth weight accounted for 6.3 percent of live births in the EU-15, as compared to 7.4 percent in the US and 8.1 percent in Japan. There does exist, however, some diversity within the EU-15, with the incidence of low birth weight ranging from 4 or 5 percent in Scandinavian countries such as Denmark, Finland or Sweden to 6 or 7 percent in France, Greece or Germany in 1998. This intra-EU-15 diversity was also confirmed by the results of the recently completed PERISTAT project (Buitendijk et alii, 2003, p. S70). On the other hand, a more substantial gap exists between the EU-15 average and the figures for some of the new EU Member States and EU Candidate Countries.

The study of the incidence of low birth weight in Europe is not problem-free. Problems stem mainly from (vital) registration. These exist for low and very low birth weights but become more serious where extremely low birth weights are concerned as the latter are not systematically registered (Buitendijk et alii, 2003). Countries are requested to follow WHO recommendations (e.g. reporting all live births and foetal losses from a minimum of 500g and 22 weeks of gestation and 25 cm body length) but legal requirements at the country level and actual practices may not always be in accordance with these recommendations (Gourbin and Masuy-Stroobant, 1993; Masuy-Stroobant and Gourbin, 1995).

1.2. Rationale

The increasing incidence of low birth weight deserves closer examination. But a more detailed investigation of low birth weight is also necessary because the mechanisms underlying its increasing incidence rank among the most important current trends in fertility behaviour. One of these trends is delayed childbearing (Bréart, 1997). In all European countries, an increase has been observed over the past decade in the proportion of live births above age 30 (Figure 3). This proportion increased from 25.6 percent in 1980 to 45.0 percent in 2001 in Norway, and from 27.4 percent in 1980 to 54.3 percent in 2001 in the Netherlands, and reached nearly 60 percent in Spain in 2000 (Council of Europe, 2003). A higher age at childbearing constitutes a risk factor for low birth weight (Appendix 3).

Table 3: Proportion of all live births above age 30 years in Europe 1960-latest



Source: Council of Europe, 2003

A separate but related factor is the increasing incidence of multiple births as a result of the increasing use of fertility treatments (Blondel et alii, 2002). The latter includes medical treatment and advice, as well as advanced clinical procedures, such as in vitro fertilization and related procedures such as oocyte donation or gamete infra-fallopian transfer (Stephen, 2000). More use is made of fertility treatments because of the higher incidence of sub-fertility or impaired fecundity.² Stephen (2000), referring to the study of Abma et alii (1997), reports that the number of women suffering from impaired fecundity in the U.S. increased from 4.5 million in 1982 to 6.2 million in 1995 and that impaired fecundity rates increased from 8.4 percent in the 1980s to 10.2 percent in 1995. There are many reasons for the higher incidence of sub-fertility or impaired fecundity, but delayed childbearing is among them.

The study of low birth weight is also important since birth weight constitutes a good indicator of the current health status of the child and a good predictor of health problems later in the child's life, which furthermore is rather easily available and reliably measured (more reliable than gestational age). This is important as, while more and more low (<2,500g), very low (<1,500g) and extremely low birth weight (<1,000g) children survive (Appendix 2), many of those who do survive – especially the very low and extremely low birth weight children – experience health problems from immediately after birth to later in life. So attempting to use perinatal variables to predict the later development of children has to be valued.³ It is not only necessary to identify in early childhood factors that cause disabilities in order to change, eliminate or lower their future impact, but also important to identify infants at risk of being disabled (Gissler et alii, 1999).

The relevance of low birth weight research is also clear from the fact that the potentially severe health consequences of very low and extremely low birth weight have given rise to a number of societal debates, which appear to split Europe right down the middle. One debate centres on ethical issues. A study by Rebagliato et alii (2000) on physicians' attitudes towards neonatal end-of-life decision-making in 10 European countries, found that those in countries such as Estonia, Hungary, Italy and Lithuania were consistently in favour of saving the lives of children at any cost, while those in the Netherlands, Sweden and the United Kingdom were more likely to take account of quality-of-life issues in their decision-making. Buitendijk et alii (2003) found that "the proportion of neo-natologists who would withhold resuscitation in the delivery room from a 24-week 560g neonate ranged from 2% in Germany to 63% in The Netherlands. Of those who would resuscitate,

² It is important to make a distinction between impaired fecundity and infertility. The former is defined as difficulty in conceiving or in carrying a child to term, and the latter as the failure to conceive for a period of 12 months or longer due to a deviation from or interruption of the normal structure or function of any reproductive part, organ or system.

³ Development refers to the physical, mental and psychomotor aspects of child development.

their opinion would change if the parents refuse resuscitation from 6% in Italy up to 40% in the UK” (p. S74). Differences of opinion and behaviour as far as neonatal end-of-life decision-making is concerned also exist between, for instance, neo-natologists on the one hand and obstetricians on the other hand.

Another debate focuses on the costs to the family and society of keeping low birth weight children alive and raising them. Neonatal hospital costs (antenatal corticosteroids, new modes of ventilation, exogenous surfactant, etc.) are high. Hospital costs for babies weighing less than 1,000g at birth were 75 percent higher on average than those incurred by babies weighing 1,000-1,499g, and more than four times higher on average than those incurred by babies weighing at least 1,500g (Petrou, 2003, p. 18 on the UK in 1998). Costs remain high after hospital discharge. The same study cites Gennaro (1996), who found that the out-of-pocket expenses incurred by a family after the discharge of a low birth weight infant from the neonatal unit amounted to US\$95/week. As children grow older costs continue to be high, though their nature may change. Direct expenses include, for instance, the cost of frequent travel to the hospital, of having to make childcare arrangements for other siblings at those times, and of attending special educational facilities later on. Petrou (2003) makes reference to a study by Chaikind and Corman (1991) indicating that children who weighed less than 2,500g at birth were 50 percent more likely to be enrolled in any type of special education than children who were of normal weight at birth (p. 19), and that the additional cost to the US educational system of educating such children was US\$322.9 million a year. There are also, however, indirect or hidden costs. Mothers of such infants and children are often not able to work, or need to reduce their working hours, which translates into lowering the family income. Caring for such infants and children also requires large amounts of physical and emotional energy.

When focusing on the child health consequences of low birth weight in European countries and on how these consequences are mediated by the social environment of the child, this paper will try to answer a number of questions: *Does the effect of birth weight on child health outcomes change after controlling for social and economic factors? Do its consequences worsen as birth weight decreases? Does the nature of the experienced health problems change as age increases?*⁴

This paper first presents a number of methodological issues related to the assessment of the health consequences of low birth weight. This is

⁴ Underlying broader research questions, which the literature overview cannot necessarily answer, include: 1. *Can a 'good' social environment protect low birth weight children from developing health problems?* 2. *Can a 'good' social environment reduce the health outcome gaps between low birth weight and normal birth weight children?* 3. *And if this is the case, does a 'good' social environment have the same potential compensating effect when it comes to very low or even extremely low birth weight children?*

followed by a discussion of actual findings on the health consequences of low birth weight. The paper concludes with a discussion of these findings.

2. Literature review

2.1. Definitions and indicators of child health

Definitions

Health is a multi-dimensional concept. WHO proposed the following definition: “A state of complete physical, mental and social well-being and not merely the absence of disease or infirmities.” Following its appearance in the preamble of the 1948 WHO Constitution, this concept has often been hailed for its comprehensiveness and its emphasis on the broader positive and psycho-social aspects of health beyond the traditional biomedical negative aspects such as death, disease and disability (Young, 1998). Subsequently, the WHO European office further adapted the above definition into: “Health is the extent to which an individual or group is able on the one hand to realize aspirations and satisfy needs, and, on the other hand, to change and cope with the environment. Health is therefore seen as a resource for everyday life, not the objective of living; it is a positive concept emphasizing social and personal resources as well as physical capacities” (ibid., p.1).

Based on these definitions, Young developed his own multi-dimensional classification scheme of the components of the health status (Table 4). He identified 4 domains: (1) opportunity; (2) perceptions; (3) functional status; and (4) impairment. Each domain is further disaggregated into sub-domains. The functional status domain comprises the (1) social, (2) psychological, and (3) physical sub-domains. It is clear from this classification that even within the functional status domain what matters is not only physical issues but also broader health issues, more linked to quality of life (participation in the community, interaction with others, happiness, etc.).

The above definitions and classification schemes concern health in general. They are not specific to child health. But in the case of child health too a multi-dimensional approach is required (Hogan and Msall, year unknown), which recognizes that child health is age-dependent. In this paper, our focus is on the development and educational disability aspects of the health consequences of the child.

Indicators

Many different measurement tools (tests) are used to assess the health consequences of low birth weight (Table 6, Column 7 provides an overview

of measurement tools used in the selected studies). These tools mainly measure outcome variables in the social and psychological sub-domains of the functional status domain in Young's classification scheme (see Table 5).

Table 4: Components of Health Status

DOMAINS	SUB-DOMAINS	DEFINITIONS/INDICATORS
<i>Opportunity</i>	Social cultural handicap	Disadvantage because of health
	Individual resilience	Capacity for health; ability to withstand stress; reserve
<i>Perceptions</i>	Satisfaction with health	Physical, psychological, social function
	General health perceptions	Self-rating of health; health concern/worries
<i>Functional status</i>	<i>Social</i>	
	Limitations in usual roles integration	Acute/chronic limitations in social roles
	Integration	Participation in the community
	Contact	Interaction with others
	Intimacy	Perceived feeling of closeness; sexual relations
	<i>Psychological</i>	
	Affective	Attitudes and behaviours; psychological distress/well-being; happiness
	Cognitive	Alertness, disorientation, problems in reasoning
	<i>Physical</i>	
	Activity restriction	Acute/chronic limitations in mobility, self-care, sleep, communication
Fitness	Performance of activity with vigour and without excessive fatigue	
<i>Impairment</i>	Subjective complaints	Reports of symptoms, sensations, pain feeling or specific health problems
	Signs	Observable clinical abnormalities on physical examination
	Self-reported disease	Reports of diagnosed medical conditions
	Physiologic measures	Laboratory data (plasma, other body fluids, tissue specimens)
	Clinical diagnoses	Physician diagnoses available in medical records, summary of review panels
<i>Death/Duration of Life</i>		Measure of mortality, survived longevity

Source: Young, 1998, pp. 62-3.

Table 5: Breakdown of the concept of health and definitions/indicators and operationalization of selected articles

<i>Functional Status</i>				
<i>Authors</i>	<i>Social</i>	<i>Psychological</i>	<i>Physical</i>	<i>Other domains</i>
1. Shenkin et alii (2001)		X		
2. Cheung (2002)	X	X		
3. Larroque et alii (2001)	X			
4. Hack et alii (1994)		X	X	
5. Saigal et alii (2003)		X		
6. Saigal et alii (2000a)		X		
7. Saigal et alii (2000b)	X	X		X (perceptions)
8. Piecuch et alii (1997)		X	X	
9. Avchen et alii (2001)		X	X	
10. Hack et alii (2002)		X	X	
11. Resnick et alii (1998)		X		
12. Resnick et alii (1999)		X		
13. Walter et alii. (2000)			X	X (impairment)
14. Boardman et alii (2002)		X		
15. Kelly et alii (2001)	X	X		
16. Gissler et alii (1999)		X		
17. Singer et alii (1997)		X		
18. Gissler et alii (1998)		X		
19. Smith et alii (2003)		X	X	
20. Vohr et alii (2000)		X	X	
21. Sweet et alii (2003)		X	X	
22. Andersson et alii (1997)	X	X		
23. Markestad et alii (1997)		X		
Total	5	21	8	2

2.2. Selection criteria

According to Wilcox (2001), about 200 articles appear each year on the subject of low birth weight. While a number of review articles exist in the area of risk factors for low birth weight (Kramer, 1987; Kallan, 1993; Shah and Ohlsson, 2002; and de Bernabé et alii, 2004), this does not appear to be the case to the same extent in the area of health consequences of low birth weight.

This is at least partially related to the fact that systematic and rigorous literature overview methodologies are lacking. Selection bias may result from the fact that the researcher does not use the right selection terms, or that the search engine does not cover a particular type of document (unpublished working/discussion papers, dissertations, etc.) As a result, we broadly agree that “one might imagine that ‘high quality’ systematic reviews, such as those that set eligibility criteria before beginning data collection, or those that mask reviewers to authors and results, might have different findings than those that did not” (Dickersin, 2002, p. 10).

Each author therefore develops his or her own step-by-step methodology to provide a comprehensive literature overview. Good examples are provided by Saurel-Cubizolles and Kaminski (1986), Amato

and Keith (1991), Shah and Ohlsson (2002), Klumb and Lampert (2004) and de Bernabé et alii (2004). The approach taken in this paper has been inspired by those authors' methodologies and the following criteria have been used to identify literature:

- Use was first of all made of the following search engines: medline; psycho file; socio abstract; current contents; and JSTOR;
- Use was then made of key words such as 'low birth weight AND child health', 'low birth weight AND developmental outcome', 'low birth weight AND educational disability, 'birth weight trends'.
- After step 2, 189 articles had been identified, a number which was reduced by answering the following questions:
 - *Is the study based on data at the single organization level, the regional level, or the population level? In this selection, studies at the population level were given precedence.*
 - *Is one of the independent variables low birth weight? And is it suitably operationalised?*
 - *Does the study take account of social determinants? Does the study address our overall research questions?*
 - *Is the dependent variable (child health/developmental outcome of the child) properly defined and operationalised also in terms of the age of the child?*
 - *Are the results statistically significant?*

In addition, since we noticed the limitations of relying solely on search engines in carrying out a literature overview, we tried to compensate for perceived weaknesses in a number of ways. This included following up key references in key articles; speaking to local experts; and making optimal use of an existing network of European epidemiologists active in the field of low birth weight (ex. EURONATAL network) by making use of their suggested studies. This resulted in the identification of an additional 786 articles.⁵ Together with the articles that were identified through search engines, a total of 975 articles were gathered. Some articles from this selection were used to provide background on the risk factors of low birth weight (Appendix 3). But for the health consequences of the child, 23 articles were carefully reviewed (Table 6).

⁵ Among which 683 articles are counted as it was recommended by the expert to the extensive list of literature presented in the web sites. See Appendix 4 for a list of experts contacted.

2.3. Assessing the health consequences of low birth weight

Before presenting actual findings, we first discuss some methodological problems, which were identified when reviewing the selected studies.

Small sample sizes: A large number of authors identify the problem of small sample sizes (Kelly et alii, 2001; Larroque et alii, 2001; Saigal et alii, 2000a/b; Saigal et alii 2003). Only about 10 percent of all studies is based on regional samples, while just 3 percent is population based (Avchen et alii, 2001). The small sample problem is exacerbated by the fact that, when carrying out longitudinal studies, samples often suffer from high attrition (drop-out) rates (Saigal et alii, 2000a/b).

Lack of or inconsistent use of control groups: Some studies do not include adequate control groups, which makes it difficult if not impossible to properly control for variables such as low birth weight (Kelly et alii, 2001; Larroque, 2001; Saigal et alii, 2000 a/b). If control groups are included, the approach taken differs from study to study hampering the comparison of research results across studies. Sometimes different groups are compared within the low birth weight population, and sometimes comparisons are made between low birth weight and normal birth weight populations.

Inconsistent operationalization of low birth weight: Categorizations of low birth weight often differ from the usual WHO categorization (Appendix 1). Table 6 shows that some authors make use of 500g increments (Shenkin et al, 2001; Cheung 2002), while other authors use a 250g/500g/1250g/1750g or even other categorizations (Resnick et alii, 1998, 1999; Hack et alii, 1994). That may be justified in some cases, but it precludes comparability.

Absence of control for neonatal care received: It is increasingly recognized that one has to control for the kind of neonatal care received immediately after birth. Neonatal intensive care treatment has changed significantly over time and also differs across hospitals. Saigal et alii (2003) report that "differences in the philosophy of resuscitation and in the aggressiveness of neonatal interventions, for example, are not often addressed, and these practice differences may affect survival and long-term outcome" (p. 943).

Inconsistent diagnosis and naming of health consequences: Avchen et alii (2001) report that "inconsistency regarding diagnostic criteria of disabilities has made it difficult to operationalise study variables and generalise findings across the literature" (p.895). On the basis of Aylward et alii (1989), they also report that different names are perhaps used for the same health consequence (e.g. 'impairment' vs. 'disability' vs. 'handicap').

Too much focus on early childhood: The focus so far has been mainly on pre-school and pre-adolescent outcomes. It has recently been recognized, however, that many health problems only appear later in life and that disease patterns change over time. Avchen et alii (2001), for instance, report that "only 29 percent of children with special needs were identified before 5 years

of age. Instead, identification of special education needs and placements tended to increase through middle childhood. Learning disabilities were not typically identified before third grade, and many other disabilities related to academic performance were not detected until a child was even older" (p. 895). Saigal et alii (2003) also found that it is difficult "to assess accurately intellectual abilities until later in childhood" (p. 943). Focusing on the health status of adolescents is also important as a better picture is provided of the capacity to function in adult society (Hack et alii, 1994).

Too much focus on neurological development: A majority of studies on the health consequences of low birth weight has focused on neurological development (Avchen et alii, 2001; Hack et alii, 1994; Larroque et alii, 2001; Saigal et alii, 2000 a/b; Saigal et alii, 2003). As the focus of studies has shifted to school age children and adolescents, "the investigation of their outcomes has evolved from a narrow focus of neurodevelopmental impairments to broader considerations of the overall morbidity" (Saigal et alii, 2000b, p. 569).

Almost exclusive reliance on health provider data: So far low birth weight studies have relied almost exclusively on data from health providers, rather than information obtained from parents, for instance. Since the shift in attention to the child health consequences of low birth weight at higher ages also requires taking a broader view of morbidity (e.g. mental aspects), such data could serve as a useful complement to health provider data (Saigal et alii, 2000b).

3. Review of health consequences of low birth weight

As discussed in the introduction, the prevalence of low birth weight has increased over the course of the last decade. The later development of low birth weight children is still not very well known, however. All studies of low birth weight agree though that, after controlling for social and economic factors, low birth weight has an independent negative effect on child health outcomes. And this effect worsens as birth weight decreases (Boardman et alii, 2002). The same observation has been made for infants 'small-for-gestational age' (SGA). The following sections discuss the independent effects of low birth weight (by birth weight category) and the role of social factors (see also Table 6 for references).

3.1. Small for gestational age (SGA)

Many studies have suggested that infants born (SGA) are at greater risk for health problems later in life than infants born 'appropriate for gestational

age' (AGA).⁶ In the early years of the child's life, these problems are mainly of a neurological nature. Later on, learning and behavioural problems become more important (Andersson et alii, 1997).

13 months: Markestad et alii (1997) tried to compare the growth patterns and psychomotor development of healthy SGA and AGA infants, and identified factors predictive of outcome at 13-14 months of age. By that age, SGA infants had showed partial catch-up in growth, but they still had smaller weight, crown-heel length, and head circumference than AGA infants. SGA children scored as well as AGA children on the motor, but lower on the mental scale.

Ages 11 and 18: Larroque et alii (2001) studied the relationship between being born SGA or AGA and school difficulties at ages 11 and 18.⁷ Compared to being AGA, being born SGA was associated with poorer school performance, even after controlling for factors such as maternal age and educational level, parental socio-economic status, family size, and gender.

3.2. Low birth weight (<2,500g)

Avchen et alii (2001) stated that "while mortality rates declined for low birth weight infants, the consequences of survival for these children may be associated with adverse developmental outcomes" (p. 895). And indeed a number of studies have established links between low birth weight and (1) problems pertaining to school performance, psychomotor development and emotional well-being, and conduct disorders in children and adolescents (Cheung, 2002); (2) problems in pulmonary function, physical growth, neurological outcome, psycho-social development and social disadvantages (Gissler et alii, 1999); and (3) respiratory problems, cognitive, neurological and psychological deficits (Kelly et alii, 2001).

Age 7: Gissler et alii (1999), in their study of whether children's health at age 7 could be predicted by perinatal health, found a clear association between poor perinatal and poor subsequent health. The best individual predictors in the study were gestational age and birth weight, though even those could not predict the health outcome sufficiently.

Ages 12-15: Avchen et alii (2001), in their study of birth weight and school-age disabilities for a population-based cohort of Florida children born between 1982 and 1984 and receiving a public school education in 1996-97, found that risk ratios for specific school-identified disabilities increased as

⁶ SGA is also referred to as intrauterine growth retardation (IUGR), no generally accepted standard definition exists: i. birth weight less than the 10th (or 5th) percentile for gestational age; birth weight less than 2500g and gestational age greater than or equal to 37 weeks; and birth weight less than 2 standard deviations below the mean value for gestational age (Kramer, 1987, p. 664).

⁷ SGA here refers to a birth weight and/or length below the third percentile.

birth weight decreased for all birth weight strata of <3,500g.⁸ They emphasized that low birth weight was mostly related to cognitive and motor development but less to learning, speech, and behaviour disabilities.

Age 26: Cheung (2002), in his study on the early origins and adult correlates of psychosomatic distress, made use of the 1970 British Birth Cohort Study and found that, even after controlling for social factors, birth weight standardized for gestational age had a "reverse J" relation with psychological distress at age 26.⁹

3.3. Very low birth weight (<1,500g)

Very low birth weight survivors are at greater risk for health problems later in life than low birth weight children. Problems include childhood neurodevelopmental morbidity, general health problems, recurrent infections and hospitalizations, poor physical growth, behavioural and attention disorders, and difficulties at school in mid-childhood, with a high proportion requiring special educational assistance (Hack et alii, 2002; Saigal et alii, 2000a/b).

Age 3: Singer et alii (1997), in their study of the developmental outcomes of infants with Bronchopulmonary Dysplasia (BPD) and very low birth weights, found that birth weight had no significant effect on motor development by age 3, once BPD and neurological risk were accounted for.

Ages 2, 5, 9-14: Walther et alii (2000), in their study of the outcomes of a Dutch national cohort of very preterm infants, focusing on 1,338 live born infants with a gestational age <32 weeks and/or a birth weight <1,500g, found that a rather small percentage of these very preterm infants (10 percent) had a severe disability or handicap at school age. However, although 90 percent of the children were without severe disabilities at school age, many of them met serious difficulties in everyday life, and the burden of mild developmental abnormalities, behavioural and learning disorders increased with age. No less than 40 percent of survivors would not be able to become fully independent adults.

School-age (6-8 years): Smith et alii (2003) examined the relationship between breastfeeding and childhood cognitive development among 439 school-age children weighing <1,500g. Higher test scores for each domain of cognitive function except memory were observed among children who were breastfed directly. A comparison with normal birth weight children was not carried out, so on the basis of this study it could not be concluded that direct breastfeeding completely makes up for deficits.

⁸ Birth weights are measured in 500g increments starting with below 999g.

⁹ This study includes live-born singletons with a GA 37-42 weeks and without congenital anomalies.

Age 20: Hack et alii (2002), in their study of outcomes in young adulthood for very-low-birth-weight infants, compared a cohort of 242 VLBW survivors with 233 controls with normal birth weights. Fewer very-low-birth-weight young adults had graduated from high school. Very-low-birth-weight men, but not women, were significantly less likely than normal-birth-weight controls to be enrolled in postsecondary study. Very-low-birth-weight participants also had a lower mean IQ and lower academic achievement scores. In addition, they had higher rates of neurosensory impairment and subnormal height.

3.4. Extremely low birth weight (<1,000g)

Extremely low birth weight children have higher mortality rates and survivors are at greater risk for health problems later in life than low and very low birth weight children. Among extremely low birth weight infants, high rates of neonatal morbidity can be found (Hack et alii, 1994). Survivors have a 20-50 percent neurodevelopmental impairment rate during early childhood (ibid.). At school, in mid-childhood, children who are ELBW are more likely to have lower IQ and academic achievement scores, experience greater difficulties, and require significantly more educational assistance than children who are born at term. They are particularly vulnerable to problems related to inattention and hyperactivity at school age (Saigal et alii, 2003). Compared with normal-birth-weight controls, fewer persons with birth weights below 1,000g graduate from high school (Hack et alii, 2002).

Age 18-22 Months: Vohr et alii (2000), in their study of the neurodevelopmental and functional outcomes of extremely low birth weight infants, found that 37 percent had a Bayley mental developmental index below 70; 29 percent had a psychomotor developmental index below 70; 25 percent had an abnormal neurological examination; 11 percent suffered from hearing impairment; and 9 percent suffered from vision impairment. It was also found that neurological, developmental, neurosensory and functional morbidities increased with decreasing birth weight.

Kindergarten: Resnick et alii (1999), in their study of the impact of low birth weight, found that both perinatal and socio-demographic factors influenced educational outcomes. Perinatal factors, in particular birth weight <1000g, had the largest effect on the need for special education (SE), whereas socio-demographic factors had a larger effect on mild educational disabilities, such as learning disabilities (LD), emotional handicaps (EH), academic problems (AP) and to some extent educable mental handicaps (EMH).

55 months: Piccuch et alii (1997), in their study of the outcome of extremely low birth weight infants (500 to 999 grams), looked at a total of 446 infants born between 1979 and 1991 and followed them to a mean age of 55 months +/- 33 standard deviations. They found that within this group, low birth weight was not associated with abnormal outcomes. The associated risk

factors for poor outcomes were specific and included intracranial haemorrhage (ICH), cystic periventricular leukomalacia (PVL), chronic lung disease (CLD) and social risk.

Age 12-15: Avchen et alii (2001), in their study of birth weight and school-age disabilities for a population-based cohort of Florida children born between 1982 and 1984 and receiving a public school education in 1996-97, found that the lightest infants born (<999g) accounted for only 0.2 percent of the population, but had a disability rate of no less than 45 percent.¹⁰ On the other hand, the heaviest children born (>5,000g) also accounted for only 0.2 percent of the population, but had a disability rate of only 18.7 percent. The majority of children (37.5 percent of the population) weighed between 3,000 and 3,499g, and this category had a disability rate of 15.9 percent (p. 896-97).

Age 12-16: Saigal et alii found in a number of studies on ELBW (2000a, 2000b) that ELBW children are in a disadvantaged position. In their study on school difficulties, differences by birth weight became apparent between age 8 and the teenage period. Parental perceptions of the health status and social competencies of adolescents were negative. Across 4 different populations - children 8 to 11 years old in New Jersey and Ontario in the US, Bavaria in Germany, and Holland (2000b) - they consistently found similar behavioural outcomes, with ELBW children requiring special educational assistance or repeating grades.

3.5. Even lower birth weights (<750g)

Many recent studies have focused on even lower birth weight survivors.

600 grams and less: Sweet et alii (2003), in their study of the age 2 outcome of infants weighing 600 grams or less at birth, found that 24% of those babies had survived and that 90 percent of the surviving infants were abnormal in neurodevelopmental terms. Major problems included cerebral palsy, blindness, gastrostomy and ventriculoperitoneal shunts.

750 grams and less compared with 750-1499g: Hack et alii (1994), in their study of school-age outcomes in children with birth weights under 750g, compared a regional cohort of 68 surviving children born from 1982 through 1986 with birth weights under 750g with 65 children weighing 750 to 1499 g at birth and 61 children born at full term. They found that those who weighed 750g and less had less cognitive ability, psychomotor skills and academic achievement as well as poorer social skills, adaptive behaviour and attention.

¹⁰ Total percentage of cases with a disability within the birth weight stratum. For details see Avchen et alii (2001).

3.6. The role of social factors

The above clearly shows that most studies of low birth weight and SGA have focused on the relationship between perinatal factors and cognitive and neurological development. Relatively little is known about other factors which are important to child health development, such as the social and home/family environment (Andersson et alii, 1997).

Nevertheless it has been suggested that the environment, especially the early home environment, plays a central role in child health and (cognitive) development. Andersson et alii (1997), for instance, have noted how the quality and amount of stimulation received by children in different environments varies greatly, care-taking practices of lower- and middle-class parents differ substantially, and children from lower-class families seem to develop more slowly. Angelsen et alii (2001) have highlighted the importance of environmental factors - such as adequate nutrition and the parental ability to create a good and stimulating home environment - and have focused on the positive correlation between breastfeeding and cognitive development in children. Further, in the study by Smith et alii (2003), where the effect of breastfeeding (which was believed to be associated with confounding socio-economic factors) on childhood cognitive development among VLBW children was examined, it was found that both expressed milk feedings and direct breastfeedings were associated with improved visual-motor function. Breastfeeding mothers were more likely to be older and married, and to smoke less.

So far, however, the role of the environment in shaping low birth weight children's health outcomes had not been studied sufficiently, or incorrectly. Andersson et alii (1997) have noted that "the relationship between cognitive development and social conditions among infants born SGA had been sparsely studied" (p. 83). On the other hand, Saigal et alii (2003) have noted that "socio-economic factors, racial and ethnic differences, the nature of funding of health care ... may further contribute to differences in the reported outcomes" (p. 943) but that quite often these are not sufficiently controlled for. Finally Kelly et alii (2001) found that one of the reasons for the existing inconsistencies between different studies on low birth weight was "not considering the impact of the social environment" (p. 88).

One of the main obstacles to properly controlling for the impact of the social environment on health outcomes is the already aforementioned usually high sample attrition rate affecting longitudinal studies. The 1970 British Birth Cohort Study, for instance, noted "the considerable sample attrition rate". Cheung (2002) referred to a study following new-born SGAs from birth to adolescence (Westwood et alii, 1983), which had a 72 percent attrition rate.

Another problem can be a strong selection effect generating an overrepresentation of lower socio-economic groups. In one study on the two-

year outcome of infants weighing 600 grams or less at birth (Sweet et alii, 2003), for instance, all mothers were of low socio-economic origin, whether measured by race, marital status, the receipt of social assistance, or tobacco use. This selection effect may stem from the fact that higher socio-economic groups are more likely to engage less in behaviour possibly giving rise to low birth weight (smoking, drinking, drugs, etc.). Furthermore, even if a low birth weight child is born to women in these groups, they may prefer not to pursue aggressive health treatments since they are better able to assess the possible negative impacts of low birth weight on later health and on their own lives.

Those findings that are available thus far on the role of the socio-economic environment tend to contradict each other. At least one study found that the socio-economic background does not matter much for child health outcomes (Hack et alii, 2002). On the other hand, Resnick et alii (1999) concluded that the impact of socio-demographic factors on adverse educational outcomes is greater than that of perinatal factors. Avchen et alii (2001) have demonstrated the independent effect of birth weight, while not denying the fact that black babies were two (2000-2499g) or three (<999g) times more likely than white babies to be small in the US. Singer et alii (1997) noted that mental outcomes at age 3 were affected by socio-economic factors such as minority status, race and lower social class. The relation with Bronchopulmonary Dysplasia (BPD) and higher rates of learning disabilities at school age in VLBW cohorts was not clear, however.

Summary synthesis

Some studies look at the relative contribution of birth weight and socio-demographic factors to health outcomes at the population level, other studies focus on the relative contribution of these factors within the group of (very/extremely) low birth weight children.

Small for gestational age (SGA): Andersson et alii (1997) found that SGA children are more vulnerable to adverse social conditions and in greater need of living in a protective environment than infants born AGA. They concluded that “based on the present findings we may suggest that SGA infants’ cognitive impairments may be both a result of their intrauterine growth retardation and/or a result of less than optimal stimulation for cognitive growth experienced in their home environments” (p. 85). Also, “the differences in cognitive competence between the two groups might be due to social differences and also possibly differences in their parents’ general intelligence” (ibid.).

Low birth weight: Resnick et alii (1999) studied the impact of low birth weight, perinatal conditions, and socio-demographic factors on educational outcomes in kindergarten. They concluded that adverse perinatal conditions resulted in severe educational disabilities, whereas less severe outcomes were

influenced by socio-demographic factors. Kelly et alii (2001) made use of the 1997 Health Survey for England to study children 4-15 years of age, and argued that both birth weight and social class had an important influence on the psychological well-being of the child. In this study, the birth weight effect was clearly mediated by social factors: social class, family structure, smoking environment, and maternal characteristics including age and General Health Questionnaire (GHQ) scores. An advantageous social environment protected against the development of behavioural problems in lower birth weight children. On the other hand, a disadvantageous social environment appeared to increase the risk of behavioural problems regardless of birth weight. Shenkin et alii (2001) focused on birth weight and cognitive function at age 11 and wanted to examine whether this relation is independent of social class. They concluded that "social class, birth weight, age, pregnancy number, and legitimacy of birth contribute some non-overlapping predictive power to cognitive function age 11 years. Birth weight and social class explain the largest amount of variance, are not significantly correlated, each make an independent contribution to IQ at age 11" (p. 193).

Very/extremely low birth weight: Resnick et alii (1998) wanted to assess, for low birth weight and sick infants hospitalized at regional neonatal intensive care units, the relationship between perinatal and socio-demographic factors on the one hand and subsequent educational disabilities on the other hand. They concluded that the educational disabilities of NICU survivors were influenced differently by perinatal and socio-demographic variables. They could not, however, present conclusions on which one mattered more.

Extremely Low Birth Weight: Vohr et alii (2000), in their study of the neurodevelopmental and functional outcomes of extremely low birth weight infants, found that factors associated with decreased morbidity included increased birth weight, female sex, higher maternal education, and white race. Piecuch et alii (1997), in their study of the outcomes of extremely low birth weight infants (500 to 999 grams), looked at a total of 446 infants born between 1979 and 1991 (a period during which neonatal care evolved substantially), and with a birth weight of 500 to 999g, and followed them to a mean age 55 months +/- 33 standard deviations. They found that low birth weight was not associated with abnormal outcomes. They did, however, find that the risk factors ICH III-IV/cystic PVL¹¹, chronic lung disease, and high social risk were associated with abnormal outcomes. Sweet et alii (2003), in their study of the age 2 outcome of infants weighing 600 grams or less at birth, found that 90 percent of surviving infants were abnormal in neurodevelopmental terms. Major problems were cerebral palsy, blindness,

¹¹ Intracranial haemorrhage (ICH) III-IV Periventricular leukomalacia (PVL)

Table 6: Description of the selected studies on low birth weight and health consequences: 1989-latest

1. Author(s)	2. Period and place of study	3. Sample studied: data set, #	4. Characteristics of the population	5. Statistical analysis	6. Birth weight (BW) and gestational age (GA) variables	7. Outcome variable	8. Results	9. Social and environmental factors taken into account
1. Shenkin et alii (2001)	* 1921-32 * UK	* Retrospective cohort study * Based on archival records, hospital data, and Scottish Mental Survey 1921/1932 * 449 live singletons for which more extensive data were available out of a larger group of 985 live singletons	* Singletons born in 1921 and traceable at age 11	* Descriptive and multivariate analysis (stepwise multiple regression analysis; structural equation modelling)	* BW: 7 cat. (<2500; 2501-3000; 3001-3500; 3501-4000; 4001-4500; 4500-) * GA: 3 cat. (<37 weeks; 37-42 weeks; 42< weeks)	* Cognitive function (Moray House Test)	* Social class and birth weight have independent effects on cognitive function at age 11 * No direct relation was found between social class and birth weight	* Maternal age; parity (total number of previous pregnancies); legitimacy of birth; exact age of the child in days; social class
2. Cheung (2002)	* 1970 * UK	* 1970 British Birth Cohort Study * Based on hospital records and interviews with mothers * 5,567 cases (main analysis) and 11,715 cases (supplementary analysis)	* Singletons born in 1970 with a gestational age of 37-42 weeks and without congenital anomalies and traceable at age 26	* ANOVA and multiple regression analysis	* BW: continuous but rounded to nearest 10g	* Psychological and somatic distress, assessed via Malaise Inventory consisting of 15-item psychological symptom scale and 9-item somatic symptom scale	* Birth weight z-scores were significantly related to psychological distress at age 26 * Somatic distress was associated with sex and adult correlates but not with BW and GA * A disadvantageous environment increases behavioural problems	* Parental social class at the time of birth * Respondent's (age 26) living arrangement, educational level, smoking habit, long-term illness

3. Larroque et alii (2001)	* 1971-78 * France (Haguenu)	* Population based registry * 236 SGA and 281 AGA	* Full term singletons born SGA in 1971-78 and full-term singletons born AGA in the same period and evaluated at age 20.6 ± 2.1	* ANOVA and odds ratios, logistic regression analysis	* Deviations in terms of BW and length from local standard growth curves used to determine SGA/AGA status	* Age at which secondary school is started (normally age 11) * Age at which the baccalaureate is started (normally age 18)	* SGAs enter secondary school later than AGAs after adjusting for social variables * SGA adolescents fail to take/pass the baccalaureate exams more than AGAs	* Maternal age at birth; number of children in the family; mother's marital status at birth; maternal education at birth; socio-economic status of parents; and maternal smoking during pregnancy
4. Hack et alii (1994)	* 1982-86 * US (6 counties in Ohio state)	* Data from 3 perinatal centers and community hospitals * 68 survivors born 1982-85 with birth weights <750g, and 65 survivors born 1982-85 with birth weights 750-1499g and full term	* Weighing 500-749g at the time of birth, admitted to NICU, and having survived until early school age	* Logistic regression analysis	* 500<750g vs. 750-1499g with full term	* Neurological and psychological abilities status and functioning at school age * IQ equivalent scores (Kaufman Assessment Battery for Children Mental Processing Composite Short Form)	* 21 % had subnormal mental abilities and 45% required special schooling * Compared to higher birth weight children, lower birth weight ones had neurosensory impairment, poorer developmental outcomes, including cerebral palsy, blindness and deafness * Major developmental outcomes are more closely associated with neonatal complications than with social disadvantage	* Maternal age, marital status, maternal race and maternal education

5. Saigal et alii (2003)	<ul style="list-style-type: none"> * 8/1984-6/1987 * US (New Jersey; Central) * 1977-82 * Canada (West Ontario) * 2/1985-1/1986 * Germany (Bavaria) * 1983 * Netherlands (national) 	<ul style="list-style-type: none"> * US: subset of Neonatal Brain Haemorrhage study, 231 children * Canada: regional hospital data, 397 children * Germany: subset of children in larger cohort from 16 Bavarian children's hospitals, 203 children * Netherlands: Selected from all children who were born before 32 weeks were completed and/or who weighed 500-1000g, 310 children 	* <1000g at time of birth and survived until age 8-11	* ANOVA and regression analysis	* Among survivors, a comparison was made between BW <750g vs. 750-1000g	* Psychometric measures: IQ test and achievement test (reading, math and spelling)	<ul style="list-style-type: none"> * School related difficulties become steadily more apparent as children progress at school * In all 4 countries, smaller children have similar survival rates and also receive special educational assistance to the same degree * Small variations exist across cohorts and countries 	None
6. Saigal et alii (2000a)	<ul style="list-style-type: none"> * 1977/82 - 1993/98 * Canada (Central West Ontario) 	<ul style="list-style-type: none"> * 150 geographically defined ELBW survivors, born in 1977-82, recruited at age 8 years old, and interviewed at age 12-16 years old, and their parents 	* ELBW (500-1000g) survivors born 1977-82, and followed up until age 12-16	* X ² analysis and stepwise multiple regression analysis	* BW: <750g vs. >-750g	<ul style="list-style-type: none"> * Wechsler Intelligence scale for children-revised (WISC-R) for cognition * Wide Range Achievement Test-Revised (WRAT-R) for academic achievement * Grade failure * Special educational assistance * School 	<ul style="list-style-type: none"> * Predictors at age 8 usefully predict performance in teen years * ELBW teenagers continue to function significantly worse in intellectual/achievement measures compared with age-matched peers * Differences in IQ and reading scores between ELBW 	* Gender of the child, family status, social class, maternal education

						difficulties * Neurosensory impairments	and normal BW children are significant at age 8 and even more so in the teen years	
7. Saigal et alii (2000b)	* 1987/92-2003 * Canada (Ontario)	* 169 geographically defined ELBW survivors and 145 normal birth weight survivors * Data rely on parental reporting	* Born with a weight 501-1000g and having survived until age 12-16 years vs. born at >2500g and full term	* ANOVA, Variance ratio test	* BW: ELBW vs. control group	* Parental perspective on the health status of the child according to 6 attributes ¹²	* Parents of ELBW children reported a higher prevalence of functional limitations in most domains (vision, mobility, cognition and self-care) * Their valuations of the child's health status were consistent with the severity of their disabilities	* Gender, age and family status of parent * Social class of teenage respondent
8. Piecuch et alii (1997)	* 1/1/1979-31/12/1991-onwards * US	* 446 infants born in 1979-91 with a birth weight <1000g and discharged from a hospital and medical centre in California	* ELBW (500-999g) infants followed until mean age 55 months +/- 33 months	*Multilevel statistical method	*BW: 5 cat. (500-599g; 600-699g; 700-799g; 800-899g and 900-999g)	* Neurological, neurosensory and cognitive outcomes	* LBW children did not have poorer outcomes * Other factors (ICH, CLD ¹³ and social risk) were more associated with abnormal outcomes	* Parental characteristics: educational status, occupation, type of health insurance

¹² Sensation, mobility, emotion, cognition, self-care and pain

¹³ Intracranial haemorrhage (ICH); chronic lung disease (CLD)

9. Avchen et alii (2001)	* 1/1/1982-31/12/1984 (birth) and 1996-97 (school performance) * US	* Two linked sets of records: (1) Database of state wide birth certificate data for 449,606 deliveries (2) Department of education 2,527,338 public school records for the 1996-97 academic year * In total 267,277 cases	* Children aged 12-15 years at the time of survey	* Odds ratio analysis	* Categorized for 500g increments from the range of <999g until 5000+ grams * No information on the GA	* Disability of children ¹⁴	* Infants with BW <999g were 22.05 times more likely than the referent group (<3499g) to be trainable mentally handicapped/profoundly mentally handicapped * Ethnicity mattered * Birth weight may be an independent predictor of later development disabilities	* Ethnicity of the child
10. Hack et alii (2002)	* 1977-79 * US (Cleveland)	* Hospital data (VLBW) and population-based selected children (NBW) * 242 VLBW (<1500g) survivors and 233 control having normal weight	* VLBW infant admitted to NICU and survived until age 20	* Logistic regression and multiple linear regression analysis	* VLBW and normal birth weight children	* Outcomes at adulthood (level of education, cognitive and academic achievement and rates of chronic illness and risk-taking behaviour) ¹⁵	* Differences are found in the child's educational attainment, intelligence and academic achievement across birth weights * VLBW children	* Socio-demographic status (maternal education status; maternal marital status; maternal race) and chronic health conditions

¹⁴ OI: orthopedically impaired; TMH/PMH: trainable mentally handicapped/profoundly mentally handicapped; EH/SED: emotionally handicapped/severely emotionally disturbed; SLD: specific learning disability; Other: hard of hearing/visually impaired dual-sensory

¹⁵ Measured by Wechsler Adult Intelligence Scale (WAISR-R) vocabulary and block design subtest measuring the verbal comprehension and perceptual organizational skills/academic skills – letter word identification and applied problems subtest measuring the verbal comprehension and perceptual organizational skills/health status – participants by means of questions concerning chronic medical, neurologic or psychiatric conditions that had lasted 12 months or longer as well as detailed questions concerning pregnancy and childbirth.

							were less likely to be enrolled in post-secondary educational programmes; had a higher incidence of chronic medical conditions; but less risk-taking behaviour (alcohol and drugs) * Socio-economic background (marital status and race) matters less for the outcome	
11. Resnick et alii (1999)	* 1985/90-1992/95 * US (Florida)	* Linked records (Florida Department of Education and Florida Vital Statistics) * 339171 records	* Children born 1985-90 and entering kindergarten in 1992-95	* Generalised logistic regression model	* BW: 7 cat. (500-749; 750-999; 1000-1499; 1500-2499; 2500-2999; 4750-6049; 3000-4749) * No info on GA	* Educational placement at kindergarten into 7 mutually exclusive SE (special education) categories	*Socio-demographic factors have a greater total impact on adverse educational outcomes than perinatal factors Children of young mothers seem to experience more educational disabilities * Adverse perinatal conditions lead to severe educational disabilities, although less severe outcomes are influenced more by the socio-demographic background	* Socio-demographic factors: ethnicity of the child; gender of the child; maternal age; maternal marital status; maternal education; poverty of the child; child prenatal care; mother's previous pregnancy experience(s) * Perinatal factors: birth weight; congenital anomalies; labour complications

12. Resnick et alii (1998)	* 1980/87-1992-93 * US (Florida)	* Linked records (medical records and educational records from the Department of Education) * 24698 children	* Children born the period 9/1980-8/1987, admitted to NICUs, and having survived until age 5-13 years	* Main effects models/Odds ratios analysis	* BW: 5 cat. (500-749; 750-999; 1000-1499; 1500-2499; 2499)	* Children with educational disabilities and 9 specific special education categories	* PI, SI, PMH and TMH ¹⁶ were influenced by perinatal factors * EMH, SLA, EH, SLD ¹⁷ were influenced both by perinatal socio-demographic factors	* Child's sex, mother's race, mother's marital status, mother's education and family income at time of birth
13. Walter et alii (2000)	* 1983 * Netherlands	* Perinatal data based on project on pre-term and small for gestational age infants (POPS) * 1338 live born	* Born <1500g with GA <32 weeks and measured at age 2, 5, 9-14 years	* Descriptive analysis	* No categorization	* Mortality, major and minor handicaps and disability at different ages	* Severe handicaps are detected at age 2 and do not disappear * 10% of these preterm infants/small children have severe disability or handicap at school age * 90 % meet serious difficulties in everyday life	None
14. Boardman et alii (2002)	* 1986-96 * US	* 1986-96 National Longitudinal Survey of Youth-Child Data * 5145 children	* Children aged 6-14 years	* Multilevel statistical method	* BW: 3 cat. (<1500g/VLBW; MLBW/1500-2499g; NBW/>2499g)	* Developmental outcomes through Peabody Individual Achievement Test of Mathematics and Reading Recognition tests	* VLBW children face greater challenges than do MLBW children in terms of positive developmental outcomes * Their home environments and the socio-economic and demographic	* Race/ethnicity of the child, child's age, sex of the child, marital status of the mother at the time of interview, poverty status of the family, and maternal education

¹⁶ Physically impaired (PI), sensory impaired (SI), profoundly mentally handicapped (PMH) and trainable mentally handicapped (TMH)

¹⁷ Educable mentally handicapped (EMH), specific learning abilities (SLA), emotionally handicapped (EH) and specific learning disabilities (SLD)

							backgrounds of their parents have much more influence on children's cognitive development than those of the birth weight * Negative effects are found but those are weaker among older children than among young ones * Other social economic effects are found to be either constant or more pronounced at age 14 than at age 6	
15. Kelly et alii (2001)	* 1997 * UK	* 1997 Health Survey for England * 5181 children	* Randomly selected children aged 4-15 years	* Multiple (least square) regression analysis	* Birth weight was rounded to the nearest 10g and transformed into Z-score.	* Psychological health by 5 dimensions of behaviour ¹⁸	* Boys' birth weight is a specific independent risk factor for hyperactivity and for girls' birth weight is a predictor of the quality of peer relationships * Presence of smokers in the home is a strong predictor of behavioural	* Maternal smoking status; social class of the head of the household; family structure; presence of smokers in the household; maternal GHQ 12 score; maternal age; gender and age of the child

¹⁸ These include: conduct problems; hyperactivity; emotional symptoms; peer relationships and pro-social behaviour.

							problems in childhood (because of a direct biological effect and also because smoking is a marker of social disadvantage) * A good social environment protects against behavioural problems	
16. Gissler et alii (1999)	* 1987-94 * Finland	* Finnish Medical Birth Register (MBR) * 60192 children	* Born in 1987 and traceable at age 7 years	* Student's t-test and X ² tests; odds ratios (OR) analysis	* BW: 4 cat. (<1499g, 1500-2499g; 1500-2499g; 25-6500g and missing)	* Children's subsequent health based on 5 measures ¹⁹	* All perinatal health indicators were strongly correlated with indicators on subsequent health and the prediction of good health was satisfactory * However, a poor perinatal situation did not necessarily predict a negative outcome * SGA and ponderal index were poor predictors of child health	None

¹⁹ 1. mortality (7 days-7 years); 2. cumulative disease index; 3. cumulative incidence of intellectual disability; 4. children receiving care support; 5. children receiving special education.

17. Singer et alii (1997)	* 1989-91 * US	* NICU hospital data * 122 children with BPD; 84 VLBW children without BPD; and 123 full-term children, and having survived until 3 years old	* VLBW with BPD; VLBW without BPD; full-term	* Hierarchical multiple regression analysis	* BW: continuous variable (grams)	* Cognitive and motor development via Mental and Motor Scales of the Bayley Scales of Infant Development	* VLBW Infants with BPD performed more poorly at all ages. * Mental retardation was associated with neurological risk, low social class and minority race and motor retardation was associated with neurological risk and BPD	* Race and social class of the child
18. Gissler et alii (1998)	* 1987-94 * Finland	* 1987 Finnish Medical Birth Register (MBR) linked for each individual with records of live births in the Central Population Register and neonatal deaths in the Death Cause Register * 59,865 newborns	* From 7 days after birth until age 7 years	* Odds ratio, logistic regression, analysis	* No categorization	* Childhood health measured by 3-level cumulative disease index and cumulative incidence of asthma, diabetes, epilepsy and intellectual disabilities	* The children in the lowest social class had the highest risk for poor health outcome both in the perinatal period and childhood * The children in the lowest social class had the most intellectual disabilities, the highest mean of hospitalization days, and received the most special education *The differences in child health were not explained by the perinatal health	* Maternal background characteristics at the time of birth: age; urbanization; marital status; previous deliveries; smoking status

19. Smith et alii (2003)	* 1991-93 * US (Massachusetts New York and New Jersey)	* Follow-up studies of the Developmental Epidemiology Network cohort (hospital based): born in one of five hospitals, survived until age 6-8 years, 439 children	* <1500g at the time of birth and aged 6-8 years	* Chi-square test and analysis of variance, regression model	* BW: continuous variable (g) * GA: continuous variable (weeks)	* Breastfeeding and cognitive function, overall intellectual function, verbal ability, visual-spatial and visual-motor skills and memory	* Directly breastfed children scored particularly higher in terms of visual-motor integration * Substantial confounding factors were observed	* Maternal age, maternal verbal ability, maternal education, cigarette smoking, marital status, annual household income, gender, multiple birth, parity, length of hospital stay (days)
20. Vohr et alii (2000)	* Born in the period 1/1993-12/1994 and assessed in the period 11/1994 and 2/1997 * US (12 different sites)	* National Institute of Child Health and Human Development (NICHD) Neonatal research network * 1151 ELBW infants aged 18-22 months	* ELBW survivors aged 18-22 months	* Logistic regression analysis	* BW: 100g birth weight intervals	* Neuro-developmental, neurosensory and functional developments ²⁰	* Among this group, 51% of the cohort had a normal neurodevelopment and sensory assessment * The study suggests that 66% and 57% of ELBW children are at potential risk of developmental or motor morbidities * Overall 70% of ELBW were walking fluently, 86% had a pincer grasp and 80% were feeding independently	* Maternal and paternal education and occupation; marital status; insurance status; income level; medical history (hearing and vision)

²⁰ Bayley Scales of Infant Development-II (Mental Scale, Motor Scale and the Behaviour Rating Scale) test was administered.

21. Sweet et alii (2003)	* 1/1994 – 12/1998 * US (Women's and Children's hospital in Los Angeles)	* NICU unit retrospective review at the hospital * 21 infants	* Born <600g and survived until age 2 years	* Descriptive statistics	* No categorization	* Neuro-developmental evaluation by using the Bayley Scales of Infant Development and a standard neurological examination * Outcomes are expressed in MDI (mental developmental index) and PDI (psychomotor developmental index) scores	* Hearing was normal; neurodevelopment outcome was poor; growth patterns were impaired	* Maternal characteristics including age, race, marital status, receiving social assistance, drug, tobacco and alcohol use
22. Andersson et alii (1997)	* Years unknown * SGA Project, Scandinavia, born in 2 sites: Trondheim; or Bergen	* Longitudinal SGA study in Scandinavia * 312 infants (142 SGA infant and 172 AGA infant)	* Born in the selected sites and evaluated at ages 7 and 13 months	* ANOVA	* Divided between SGA and AGA group	* Assessment of infants' cognitive abilities through Fagan Test of Infant Intelligence (FTII) and Home screening questionnaire (HSQ) among mothers	* SGA infants are vulnerable to both poor growth and adverse social conditions * SGA infants are also more susceptible to environmental conditions than the AGA * Cognitive competence between 2 groups are more due to social differences (parental intelligence)	* Home environment, a measure of the quality of stimulation and support available to the child

23. Markestad et alii (1997)	* Years unknown * SGA Project, Norway and Sweden	* Population based data * 594 children (265 SGA and 329 non-SGA infants)	* Survived and age 13-14 months	* ANOVA; logistic regression analysis	* Mean birth weight; SGA ²¹	* Bayley Scale of Infant Development	* IUGR in healthy infants born at term has small but negative effect on growth and developmental outcomes during infancy * Mental development is particularly vulnerable to fetal starvation	* Education and maternal smoking
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²¹ In this study, SGA is defined as birth weight less than the 15th percentile for gestational age according to sex-specific Norwegian growth standards based on LMP and adjusted for parity.

gastrostomy, and ventriculoperitoneal shunts. In this study all of the mothers were of low socio-economic status, which was clearly associated with poor infant outcome. On the other hand, Hack et alii (1994), in their study of school-age outcomes for children with birth weights under 750g, concluded that social disadvantage was not associated with major developmental impairment.

4. Discussion and conclusion

This paper started with a discussion on the importance of research on low birth weight by pointing to its increasing prevalence (even though measurement problems exist), its connection with recent fertility trends (e.g. delayed childbearing and multiple births resulting from the use of fertility treatments), and the various ethical and socio-economic debates that are waged on neonatal life decision-making and on the costs for families and societies of raising possibly severely handicapped low birth weight children.

Studies of low birth weight have been hampered by a number of methodological problems. These include too small sample size; inadequate comparison groups; inconsistent operationalisations of low birth weight; a lack of controlling for differences in neonatal intensive care unit treatment; inconsistencies in both the diagnostic criteria for and the terminology on health consequences; an excessive focus on early childhood and neurological development; and an unwarranted reliance on health provider data.

Nevertheless it has been possible to establish a negative relation between low birth weight and child health outcomes. Low birth weight has an independent effect on child health outcomes, even after controlling for social factors, and this effect worsens as birth weight decreases (to VLBW and ELBW). A 'good' social environment can have a protective effect, more so for LBW than for VLBW and ELBW. Properly assessing the role of social factors is difficult, however, because of the persistence of the initial selection effect (lower socio-economic groups are more likely to engage in behaviour likely to give rise to low birth weight and are more adamant about keeping their children alive at all cost). A further reason lies in the complex interaction effects between behavioural, health-related and socio-demographic factors. This complexity is already present during the prenatal stage and at the time of birth (risk factors for low birth weight) and continues to be an underlying factor determining the health outcomes of the child thereafter.

The fact that studies of LBW increasingly take on a longitudinal nature, focusing not only on infant and early childhood health outcomes at one point in time but also on school age and adolescent outcomes from a longitudinal and dynamic perspective; the fact that the research focus has been shifting from purely neurological to broader cognitive, mental and social aspects; and the fact that the need is increasingly recognized for

making use of a broader range of data going beyond health provider data, argue in favour of making use of the life course or similar approaches.

The micro-level life-course approach proposed by Elder (1992) and Giele and Elder (1998) is in accordance with Coleman's methodological individualism (1990). Their life course framework (Giele and Elder, 1998, p. 10) allows for an understanding of how an individual's behaviour is determined by the context in which that individual is situated as well as that individual's personal history and for an insight into the causal mechanisms underlying observed behavioral outcomes. Two important operational concepts in the life course framework are those of 'location in time and place' and 'linked lives' (Giele and Elder, 1998), which draw attention to the society specificity and the cohort specificity of behaviour respectively. To study characteristics at the population level, the cohort effect (Ryder, 1965) is considered crucial. Both 'location in time and place' and 'linked lives' are captured through 'time' (age, period and cohort) (for a further explanation see Giele and Elder, 1998).

The potential of the life course approach for the study of disease has been increasingly recognized. Such a life course perspective, combining the structural and temporal aspects of determinants, is not new in the field of epidemiology. Ben-Sholmo and Kuh (2002), for instance, offer a conceptual model for the study of chronic disease. A life course perspective has also been taken by Wadsworth (1997), offering a glimpse of the complexity of handling socio-demographic factors in the study of the health consequences of low birth weight: *Although biological programming may have a deterministic effect on the range of adult health parameters, the social and family circumstances of childhood are the beginnings of pathways which will be protective to health or increase vulnerability to ill health* (p. 867). He continues by saying that *the social factors that affect both biological programming and the social and educational pathways from childhood to adulthood socio-economic circumstances, vary with historical time, and so the extent of health inequality in actuality and in potential in a cohort of a given age is likely to be different from that of a cohort of another age* (p. 867). Regardless of birth weight, childhood social and educational factors are strongly associated with adult mental and physical health outcomes, and with adult health-related behaviour. The observed long-term effects of early life physical development do not constitute inevitable outcomes of childhood development, but are mediated by *the chain of social factors that also begins in early life* (Wadsworth and Kuh, 1997, p. 2).

5. References

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Appendix 1: The definition of low birth weight

The WHO 2,500 grams criterion for the definition of low birth weight mentioned at the beginning of the paper is quite arbitrary. There exists a significant relationship between the mean height of mothers in a population and the mean birth weight of children in that same population. Therefore, if the standard WHO criterion is applied, populations with shorter women will almost by definition have a higher proportion of low birth weight. In those populations, the 'optimal' birth weight, defined as the birth weight at which mortality is lowest, is different from the European one. This is noticeable when one compares for instance countries like Portugal, Italy, Spain and Great Britain, where the average maternal height is between 1.61 and 1.63 meters, with countries like Denmark, the Netherlands and Germany, where the average maternal height is between 1.67 and 1.69 meters (Lack et alii, 2003). The relationship is also noticeable when comparing Europe as a whole with non-European populations. The study of Vangen et alii (2002), which compared the birth weight and perinatal mortality of Vietnamese, Pakistani, Norwegian and North African babies, found that mean birth weights were lower for Vietnamese and Pakistani children and higher for Norwegian and North African mothers.²²

Another comment relates to the fact that, for quite a long time, low birth weight and premature birth (defined as a gestational age of less than 37 weeks - Kramer, 1987) were used as synonyms. This gave rise to confusion (Wilcox, 2001). It has now been recognised, however, that not all premature births result in low birth weight and that not all low birth weights result from premature births. In the latter case, the terms intrauterine growth retardation (IUGR) or small-for-gestational age (SGA) are used - defined as "birth weight less than 10th (or 5th) percentile for gestational age; birth weight less than 2,500g and gestational age greater than or equal 37 weeks; and birth weight less than 2 standard deviations below the mean value for gestational age" (Kramer, 1987, p. 664). The fact that a distinction is made between SGA and other low birth weight babies already points to differences in health consequences for the two groups.

The reason why it has become possible to make this distinction more precisely is that the measurement of gestational age, while still not perfect, has greatly improved recently, with an increased use of both the last menstrual period approach (LMP - self-reported) and ultra-sound techniques (Foix-L'Helias and Blondel, 2000) (For a discussion on the technical measurement of GA see Yang et alii, 2002²³ and Lack et alii, 2003²⁴).

²² North African mothers have fewer children with low birth weight when they migrate. This is considered to be an epidemiological paradox.

²³ Yang et alii (2002) note that gestational ages measured through an EUS-scan are lower on average than those measured via the LMP-method, resulting in a higher rate of preterm birth and

Appendix 2: Mortality

Over the past few decades, the chances of survival for low birth weight children have improved significantly. This is reflected in the decrease in overall infant mortality rates, which is mainly due to decreasing mortality for the lowest birth weights. Data from the WHO 'Health for All' database show that foetal, neonatal and infant mortality rates have been decreasing over the past few decades in the EU-15. However, while neonatal and infant mortality rates are clearly converging, this does not yet appear to be the case for foetal mortality rates.²⁵ In the 10 new EU Member States too all three mortality rates are broadly decreasing, but at higher levels than the EU-15, and with as yet much less convergence.²⁶

Reductions in low birth weight mortality have greatly contributed to the decrease in overall mortality. Avchen et alii (2001) note that reduction in infant mortality was associated with an increased survival of infants in the lowest tail of the birth weight distribution. Gissler et alii (1999) note that weight-specific mortality (for low birth weight children) has decreased in the 1990s. Hack et alii (1994) note that "during the past decade, advances in perinatal care have resulted in increases in the survival of extremely small and immature infants. Whereas few infants with birth weights below 750g were actively treated before the 1980s, treatment is now accepted practice for most infants born in North America with birth weights of at least 500g, those born at 24 or more weeks' gestation, or both" (p. 753). Piecuch et alii (1997) note that "during the last decade, tertiary centres have reported decreasing mortality for extremely low birth weight (ELBW) infants. Declining mortality rates have been most dramatic for the smallest infants, specifically those of <750g birth weight" (p. 633). Forssas et alii (1998) note that the largest decline in stillbirth mortality occurred among those weighing below 1,000g, while for early neonatal deaths the group most affected weighed 1,000-1,499g at birth.

One has to be careful when discussing death rates, however. There is still substantial underreporting of stillbirths and early neonatal deaths. This was convincingly demonstrated though the recent PERISTAT project

a lower rate of post-term birth. The usual explanation for this systematic difference includes inaccurate reporting of the last normal menstrual period and the more frequent occurrence of delayed rather than early ovulation. While its conclusions are not completely definite, this study indicates that "EUS-scan-based estimates are more valid on average than LNMP-based estimates (p. 435)".

²⁴ According to Lack et alii (2003) the use of ultrasound decreases the proportion of reported post-term pregnancies and increases the proportion of preterm babies, implying the underestimation of gestational age.

²⁵ For more details on this issue see Gourbin and Stroobant (1993).

²⁶ Caution is required for cross-country comparisons since reporting and legal practices differ at the country level.

(Macfarlane et alii, 2003), for instance, for the Netherlands and Greece. Underreporting is largely due to country differences in registration practices. It can also be caused by omissions from civil registration, because births and deaths of non-residents or non-citizens are not recorded.

Appendix 3: Risk factors for low birth weight

Risk factors for low birth weight are also likely to be determinants mediating the health consequences of low birth weight after birth. We distinguish in our discussion of risk factors as much as possible between risk factors for prematurity and risk factors for IUGR (Kramer, 1987).

A. Analytical frameworks

A number of authors have developed analytical frameworks for risk factors for low birth weight.²⁷ The one most often referred to is that of Kramer (1987), even though that of Kallan (1993) appears to be more comprehensive and operational.

Based on a meta-analysis and critical assessment of the English and French language medical literature published over the period 1970-84, Kramer (1987) presents a synthesis comprising 43 potential maternal risk factors for low birth weight grouped into 7 categories: (1) genetic and constitutional factors; (2) demographic and psychosocial factors; (3) obstetric factors; (4) nutritional factors; (5) maternal morbidity during pregnancy; (6) toxic exposures; and (7) antenatal care.

The Kallan (1993) framework comprises 11 'intervening variables' (maternal characteristics) grouped into 4 categories: (1) socio-demographic (age; education; marital status); (2) health-related (parity; prior history of foetal loss or low birth weight; hypertension; diabetes; pelvic infectious disease); (3) attitudinal (wantedness of the pregnancy); and (4) behavioural (smoking; prenatal care).

Both frameworks deserve a careful assessment - even though Kramer, for instance, admits that nearly 75% of the causal factors for prematurity cannot be identified (Kramer, 1987, pp. 717-24). Both frameworks provide a comprehensive overview of risk factors and group them into suitable categories, while also acknowledging that the causes for prematurity and IUGR respectively are different. However, the direct and indirect effects of certain factors (e.g. the direct biological effect of smoking and smoking as a marker of social disadvantage) are not well explained. Furthermore, neither framework distinguishes between risk factors by birth weight category (low vs. very low vs. extremely low birth weight). Little

²⁷ E.g. Shah and Ohlsson (2002), Foix-L'Helias and Blondel (2000), and Forssas et alii (1999).

account is also taken of combined maternal characteristics, such as low parity at high age. Paternal characteristics or the timing of the onset of menarche are also disregarded.²⁸

Both authors have been able to assess the relative importance of each risk factor. According to Kramer (1987) the ranking is as follows for IUGR: *cigarette smoking; low caloric intake or weight gain; low pre-pregnancy weight; primiparity; female sex of the child; short stature; non-white race; maternal LBW and prior LBW history; general morbidity; other (together accounting for an almost complete explanation)*. And the ranking is as follows for prematurity: *cigarette smoking; prior prematurity and spontaneous abortion; low pre-pregnancy weight; and in utero exposure to diethylstilbestrol; unknown (together accounting for a 1/3 explanation)* (see, p. 717-23).

According to Kallan (1993) the most important intervening variables between race and preterm birth are: *parity; prior LBW; hypertension; and pelvic inflammatory disease (PID)*. The most important intervening variables between race and IUGR are: *marital status; prior LBW; pregnancy wantedness; and smoking*.

In short, the risk factors for IUGR are fairly well understood, while that is less the case for prematurity. There exists more clarity when it comes to the role of behavioural and health factors, while the role of socio-demographic factors is still part of the big unknown. It is because of this reason that we start our more detailed discussion of risk factors with the former ones, and keep the discussion of socio-demographic factors to the end.

B. Behavioural risk factors

Smoking: As already pointed out, smoking is an important risk factor. Jaakkola and Gissler (2004), in their attempt to assess whether there exists a causal relation between maternal smoking and asthma at age 7, studied the 1987 Finnish cohort of singleton births, and found that the risks for low birth weight, SGA, and preterm delivery were strongly related to maternal smoking during pregnancy. Zarén et alii (1997), examining the effect of maternal smoking on the relationship between maternal haemoglobin levels and pregnancy outcome, analysed data on Swedish and Norwegian women coming to antenatal care from before 17 to after 37 weeks between January 1986 and March 1988. They found that maternal smoking negatively affects foetal growth. In another article, based on the same population and study design, Zarén et alii (2000), found that maternal smoking affects male and female foetuses differently. Male and female foetuses of smoking mothers

²⁸ For paternal factor see differing views by Rychtaříkova, Gourbin and Wunsch (2004) and Basso et alii (1999); for menarche see Coall and Christholm (2003).

had mean birth weights lower by 316g and 177g respectively compared to foetuses of non-smoking mothers.

Alcohol: Larroque et alii (1995), in their article on moderate prenatal alcohol exposure and psychomotor development at preschool age in France, refer to a number of studies finding associations between moderate alcohol consumption and decreases in birth weight.

Stress: Copper et alii (1996), in a psychosocial assessment study at 25 to 29 weeks of gestation, and based on an analysis of data from the Maternal-Fetal Medicine Units Network of the National Institute of Child Health and Human Development between October 1992 and July 1994, found that after adjusting for maternal demographic and behavioural characteristics, stress was associated with spontaneous preterm birth and low birth weight.

Coffee: Vik et alii (2003), in their study in Norway and Sweden of enrolments that took place between 1 January 1986 and 31 March 1988 of women at either parity 1 or 2, of Caucasian origin, singleton pregnancy and registered before the 20th week of gestation, found that a high caffeine intake in the third trimester of pregnancy was associated with an increased risk of SGA. The increased risk was only found for male foetuses, not for female foetuses. The association held even after controlling for smoking.

C. Health-related risk factors

Abortion: A distinction has to be made between spontaneous and induced abortion. Based on an analysis of the Danish population registry over the period 1980-1992, Basso et alii (1998) found that a prior spontaneous abortion constitutes a risk factor for both very preterm and preterm delivery, even though spontaneous abortion and preterm delivery themselves also appear to share some risk factors. Another study by Henriët and Kaminski (2001), on the basis of the 1995 French national perinatal survey, found that women who had experienced induced abortion had a higher risk of preterm delivery. Identical results were obtained by Foix-L'Helias and Blondel (2000) on the basis of a nationally representative sample for the years 1981 and 1995. When controlling for other maternal characteristics, a woman was more likely to have a preterm delivery if she had had at least one prior induced abortion.

Sub-fecundity and fertility treatment: A clear link has been established between fertility treatments, also called artificial reproductive technology (ART), and multiple births. In countries such as Canada, France and the US, it has been found that “estimates based solely or partly on data from surveys or registers showed that in the late 1980s and in the 1990s, between 20% and 40% of triplet deliveries followed ART, and all in all, that about three quarters of triplet deliveries occurred after procedures for sub-fertility” (Blondel et alii, 2002, p. 1327). Similar evidence that fertility treatments increase the likelihood of multiple gestation (twins, triplets), or of sole

surviving singletons from an initially larger group of foetuses, was found by Schieve et alii (2002). Also Macfarlane et alii (1990) found in their study on the UK in the years 1980 and 1982-85 that there exists a strong association between infertility treatment and the occurrence of multiple births: 55 percent of mothers of quadruplets and above and 31 percent of the mothers of triplets had undergone some form of gynaecological investigation for infertility compared to only seven percent of mothers of twins and under three percent of mothers of singletons (p. 47).

Multiple gestation increases the likelihood of low birth weight. This is the case for twins. For example, “the risks of very preterm delivery and very low birth weight attributable to twins were higher than the risks of overall preterm delivery or low birth weight” (Blondel et alii, 2002, p. 1327). But this is also the case for triplets, quadruplets and higher order multiples. Schieve et alii (2002) found that the proportion of low birth weight among those who underwent assisted reproductive technologies in the US 1996-97 was 13.2 percent among singletons and nearly 100 (!) percent among quadruplets or higher order multiples. Singletons were more likely to be low birth weight when originally more than 2 foetuses were found by ultrasonography (p. 733).

Hypertension: Hypertension is also considered to be a risk factor mainly for IUGR, although more study is required to verify this. Studying French data for the years 1991 and 1993, Haelterman and his colleagues (1997) found that chronic hypertension has an impact on having a small child. In their analysis, the mean birth weight decreased by 161g for women with chronic hypertension compared to other women.

D. Socio-demographic risk factors

Finally, attention has to be paid to socio-demographic factors such as age, marital status and education. These are highly complex. They have their own independent effect. They also interact among themselves, however (e.g. age, education and class interact with each other). Furthermore, they interact with behavioural and health related factors.

Age: Maternal age constitutes an important risk factor. Foix-L’Helias and Blondel (2000) found that in France a maternal age above 34 years old constituted an important risk factor in both 1981 and 1995 while a maternal age below 20 years constituted an important risk factor in 1981 but not in 1995. Similar results were obtained by Dičkute et alii (2004), who in their study of Lithuania in 2001-2 identified a U-shaped relationship between maternal age and LBW risk (younger than 20 years and 35 years and older), although other factors also clearly played a role.

The importance of a young maternal age appears to be decreasing in European countries. In countries where the proportion of young mothers is

small (below 3 percent), examples being France, Finland and Sweden in the 1990s, there is no (or only a weak) association between young maternal age and pre-term birth (Foix-L'Helias and Blondel, 2000, referring to i.a. Hemminki and Gissler, 1996).

On the other hand, as Foix-L'Helias and Blondel and others have demonstrated, a higher maternal age (e.g. above 34 years old) remains an important risk factor. Other authors have also found a strong relation between a higher maternal age and the risk for premature birth. An Italian study (Astolfi and Zonta, 2002) has found that the 35 plus age group always has a significantly higher risk of still or preterm birth, or low birth weight at term, even when parity and education variables are controlled for. A French study (Bréart, 1997) has similarly found negative consequences of delayed childbearing (35 plus) in the format of higher fetal death rates (p. 72). Similar findings were also reported for Alberta, Canada, where Tough et alii (2002) reported that "when only those age 35 and older of first parity were considered, the contribution to the population increase in LBW and preterm delivery was less than half of the total contribution for this age group (36%) (p. 3 of 9). The negative effect of a higher maternal age can be weakened by education and parity, but only to a rather small extent (Astolfi and Zonta, 2002, referring also to the Danish case-study of Basso et alii, 1997).

The multi-dimensional role of age on low birth weight is shown below.

a. 'Independent effect' of age: Age first of all has an 'independent effect'. Tough et alii (2002) report that "it has been suggested that fecundability (the ability to conceive) and fertility decrease with maternal age, whereas conception delay increases. With advanced maternal age may be an impaired functional capacity of uterus, biological aging, and synergistic effects related to systematic disease" (page 5 of 9).

b. Age and smoking: In addition, age interacts with *behavioural risk factors* such as smoking. As already mentioned above, smoking has an independent effect, but smoking may also be more prevalent in particular age groups. Jakkola et alii (2001) found that smoking during pregnancy remained constant in Finland between 1987 and 1997, but that smoking itself had increased. According to their findings, the smokers were young (below 20 years), single and less educated, and mainly living in the North and East of the country.

c. Age and abortion: Age also interacts with *health-related risk factors* such as a prior experience of induced or spontaneous abortion or preterm delivery. The older a woman is the more likely she is to have had such experiences compared to a younger woman. Henriët and Kaminski (2001) found that women who reported previous induced abortions were *significantly older*, had a higher number of previous pregnancies and a obstetric history of adverse pregnancy outcome, were alone, unmarried, of non-French

nationality, of low educational attainment level, not working during pregnancy and smokers. Mothers with a high number of induced abortions were at higher risk, although no distinction was made in this study by the kind of technique used for the abortion.²⁹

d. Age and hypertension: A *health-related risk factor* such as hypertension is also associated with age. Haelterman et alii (1997) found that chronic hypertension increases above age 30.

e. Age and fertility treatment/medical assisted reproduction (MAR): Another way in which high maternal age is associated with the risk of low birth weight is through the use of fertility treatments resulting in multiple births (see above). In the case of fertility treatment, age interacts with other *socio-demographic risk factors*, such as education and class. It is only older and well-off women who can afford fertility treatment. Stephen (2000), referring to the high financial cost of treatment, notes the small number of women who can afford fertility treatment, and quotes Abma et alii (1997) as saying that actually only 3 percent of women aged 15-44 take ovulation drugs and only 1 percent utilises reproductive technologies such as intrauterine insemination, in vitro fertilization (IVF), etc. Further, when it comes to fertility treatment, age interacts not only with the *socio-demographic risk factors* education and class, but also with the *socio-demographic risk factor* marital status. It is almost only married women who seek treatment. In the case of Europe, Olsen and others (1998) found out that more married women undergo treatment.

Finally, age also interacts with the *health-related risk factor* parity. Based on their study of the 1991 Finnish Birth Register, Hemminki and Gissler (1996) found that low birth weights and pre-term births are mainly found among old primiparous women. Older multiparous women also experienced high proportions of low birth weights and preterm births but the effect was smaller than for older primiparous mothers. In addition to the usual characteristics, the study concluded that these women were urban oriented, and had miscarriages and induced abortions in their obstetric histories.

Education: Another socio-demographic factor is education. Most studies conclude that higher levels of maternal educational attainment lead to better pregnancy outcomes. Raum et alii (2001) examined the influence of maternal education on IUGR in two different political and social systems, West and East Germany in 1987/88 and 1990/91 respectively. They found that mothers among the lowest category of education in both West and East Germany had an unadjusted relative risk of 2.5 for delivering an SGA child compared to

²⁹ In France, two methods are used for legal abortions: surgical abortion (vacuum aspiration followed by curettage) and prescription of abortion pills mifepristone (RU-486) and prostaglandins for < 7 weeks gestational age. Intervention at high gestational age is low (4% after 11 weeks) in France (Henriet and Kaminski, 2001, p.1041).

those of the highest education category. This indicates that the education of the mother is a proxy for the socio-economic and lifestyle status, including smoking behaviour, frequency of prenatal care visits (health seeking behaviour), etc.

Marital status: Another socio-demographic factor is marital status. Foix-L'Helias and Blondel (2000) found that risk factors included being single in 1981 but not in 1995. So at the country level, the importance of being single as a risk factor appears to decrease over time in France. In countries with a high proportion of non-married mothers there is no association between marital status and pre-term birth. Examples of such countries are Finland, Sweden and France in 1995 (Foix-L'Helias and Blondel, 2000, referring to Rantakallio and Oja, 1990; Hemminki and Gissler, 1996; Villeneuve-Gokalap, 1990; Toulemon, 1996). In countries with a small share of extra-marital births, both cohabitation and single motherhood are important risk factors for premature birth (Zeitlin et alii, 2002). Thus, obtaining a better insight into a country's historical nuptiality pattern may throw light on low birth weight patterns. It is interesting to note, for instance, that cohabitation (living with a partner) has a longer history of wide acceptance in Finland than in many other countries. In France, for instance, cohabitation was largely restricted to the working classes in the 1970s, but became more accepted in the 1980s regardless of socio-economic background.

Social class: The socio-demographic risk factor of class interacts with behavioural risk factors such as smoking. This is demonstrated by inter alia Kramer et alii (2000) Many times, the socio-demographic risk factor of class is treated together with education and marital status. Dičkute and his colleagues (2004), based on a study of Lithuania in 2001-2, found that there exist a U-shaped relationship between maternal age and LBW risk (younger than 20 years and 35 years and older) but clearly say that low birth weight is associated with other factors: low levels of education, unstable marital status, and low income. However, the role of socio-economic status is very complex. A good example is its interaction with selection and screening processes. On the one hand, Carlson et alii (1999) and Carlson and Hoem (1999), by focusing on trajectories of foetal loss in the Czech republic, identify pregnancy outcomes that are more positive for low than for high socio-economic status women, in the format of the 'survival paradox'. On the other hand, Khoshnood et alii (2004) report in their study based on the French National Perinatal Survey of 1998 on the better access of high socio-economic status women to maternal serum screening for Down syndrome, and thus, to more informed decision-making as compared to low socio-economic status women.

Appendix 4: Acknowledgements

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