Social inequalities in pregnancy outcomes and early childhood behaviour

The Generation R Study

Pauline W. Jansen

ACKNOWLEDGEMENTS

The Generation R Study is conducted by the Erasmus MC – University Medical Center Rotterdam in close collaboration with the Erasmus University Rotterdam, School of Law and Faculty of Social Sciences; the Municipal Health Service Rotterdam area, Rotterdam; the Rotterdam Homecare Foundation, Rotterdam; and the Stichting Trombosedienst & Artsenlaboratorium Rijnmond (STAR), Rotterdam. We gratefully acknowledge the contribution of the participating pregnant women and their partners, general practitioners, hospitals, midwives and pharmacies in Rotterdam. The first phase of the Generation R Study is made possible by financial support from: Erasmus MC – University Medical Center Rotterdam; Erasmus University Rotterdam; and the Netherlands Organization for Health Research and Development (ZonMW).

The studies presented in this thesis were supported by an additional grant from the Netherlands Organization for Health Research and Development (ZonMW "*Geestkracht*" program 10.000.1003).

Financial support for the publication of this thesis was provided by The Generation R Study, the Department of Public Health, the Department of Child and Adolescent Psychiatry (all Erasmus MC – University Medical Center Rotterdam) and by the J.E. Jurriaanse Stichting.

ISBN: 978-90-8559-580-9
LAYOUT: blue in green, Jan van Wessel
PRINTING: Optima Grafische Communicatie, Rotterdam, The Netherlands
COVERPHOTOS: iStockphoto

Social inequalities in pregnancy outcomes and early childhood behaviour

The Generation R Study

Sociale ongelijkheden in zwangerschapsuitkomsten en gedrag in het vroege leven

Het Generation R Onderzoek

PROEFSCHRIFT

Ter verkrijging van de graad van doctor aan de
Erasmus Universiteit Rotterdam
op gezag van de
rector magnificus

Prof.dr. H.G. Schmidt

en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op
vrijdag 4 december 2009 om 13:30 uur

door

Pauline Wendela Jansen

geboren te Vlissingen

PROMOTIECOMMISSIE

Promotoren: Prof.dr. J.P. Mackenbach
Prof.dr. F.C. Verhulst

Overige leden: Prof.dr. H.A. Moll
Prof.dr. C. Power
Prof.dr. W.A.M. Vollebergh

Copromotoren: Dr. H. Raat
Dr. H. Tiemeier

Paranimfen: Miranda Geelhoed
Sabine Roza

CONTENTS

MANUSCRIPTS BASED ON THIS THESIS

CHAPTER 2.1
Silva LM, Jansen PW, Steegers, EAP Jaddoe VWV, Arends LR, Tiemeier H, Verhulst FC, Moll HA, Hofman A, Mackenbach JP, Raat H.
Mother's educational level and fetal growth; the genesis of health inequalities.
Revision: International Journal of Epidemiology, September 2009.

CHAPTER 2.2
Jansen PW, Tiemeier H, Jaddoe VWV, Hofman A, Steegers EAP, Verhulst FC, Mackenbach JP, Raat H.
Explaining educational inequalities in preterm birth. The Generation R Study.
Archives of Diseases in Childhood – Fetal and Neonatal Edition. 2009 Jan; 94(1): F28-F34. Epub 2008 Jun 18.

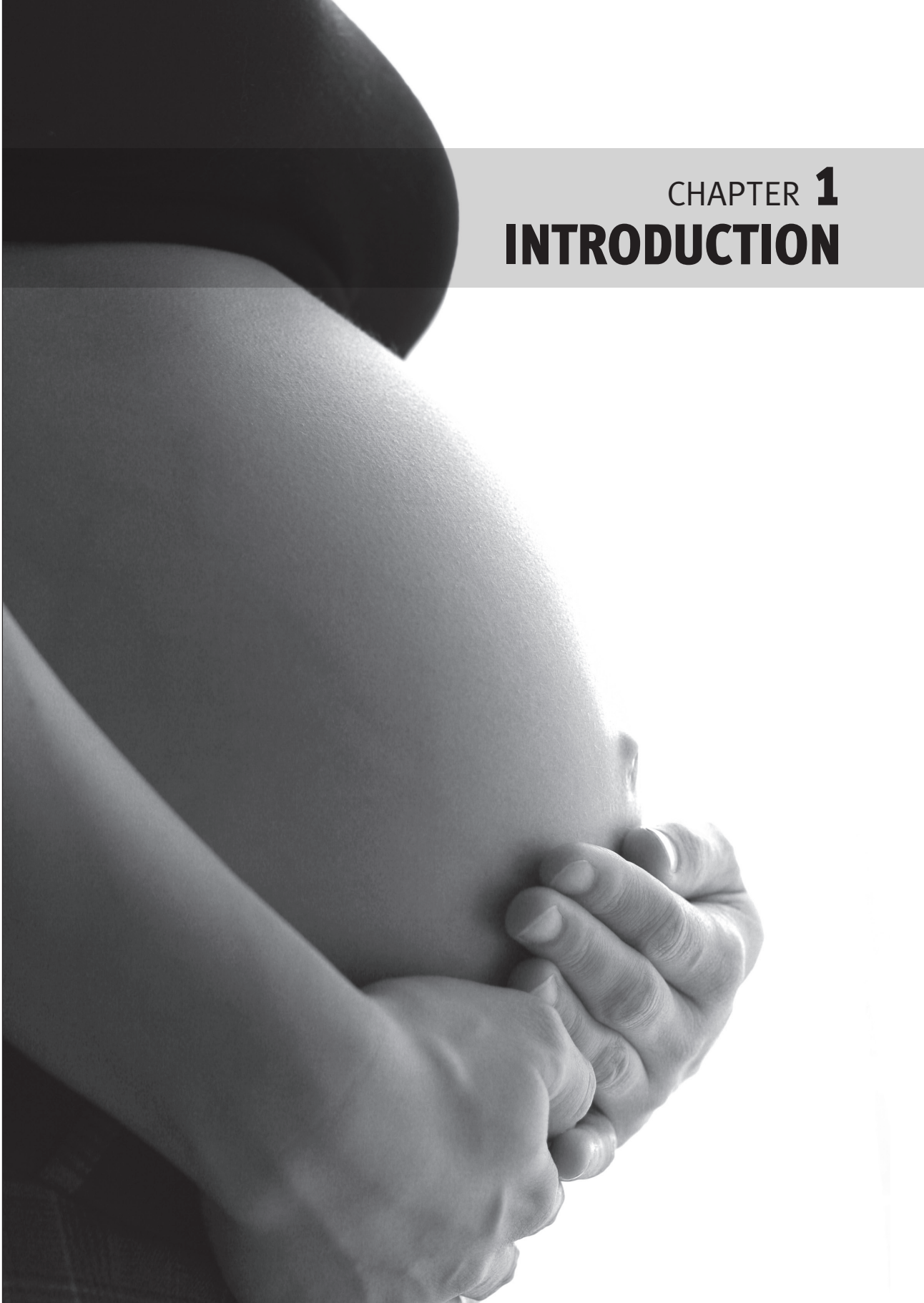
CHAPTER 2.3
Jansen PW, Tiemeier H, Looman CWN, Jaddoe VWV, Hofman A, Moll HA, Steegers EAP, Verhulst FC, Mackenbach JP, Raat H.
Explaining educational inequalities in birthweight. The Generation R Study.
Paediatric and Perinatal Epidemiology. 2009; 23(3): 216-228.

CHAPTER 2.4
Jansen PW, Tiemeier H, Verhulst FC, Burdorf A, Jaddoe VWV, Hofman A, Moll HA, Steegers EAP, Verburg BO, Mackenbach JP, Raat H.
Employment status and the risk of pregnancy complications. The Generation R Study.
Accepted for publication: Occupational and Environmental Medicine, September 2009.

CHAPTER 3.1
Jansen PW, Raat H, Mackenbach JP, Jaddoe VWV, Hofman A, Verhulst FC, Tiemeier H.
Socioeconomic inequalities in infant temperament. The Generation R Study.
Social Psychiatry and Psychiatric Epidemiology. 2009 Feb; 44(2): 87-95. Epub 2008 Jul 28.

CHAPTER 3.2
Jansen PW, Raat H, Mackenbach JP, Jaddoe VWV, Hofman A, van Oort FV, Verhulst FC, Tiemeier H.
National origin and behavioural problems of toddlers: the role of family risk factors and maternal immigration characteristics.
Revision: Journal of Abnormal Child Psychology, August 2009.

CHAPTER 3.3
Jansen PW, Raat H, Mackenbach JP, Hofman A, Jaddoe VWV, Bakermans-Kranenburg MJ, Van IJzendoorn MH, Verhulst FC, Tiemeier H.
Early determinants of maternal and paternal harsh discipline.
Submitted, September 2009.



CHAPTER 1

INTRODUCTION

The social position of individuals in a society is associated with health and disease throughout the whole life span, with persons further down the social ladder being worst off.[1-4] Social position encompasses different aspects such as material and financial resources, knowledge, social support, and housing conditions. In scientific research, low social position is often indicated by low income, low education, unemployment, single or teenage parenthood, neighbourhood disadvantage, or ethnic minority status. In this thesis, we study a few indicators of unfavourable social positions. The collective of these indicators is referred to as "social disadvantage".

During the past decades, numerous studies in both Western and non-Western countries have indicated large health inequalities between socially advantaged and disadvantaged people.[1-4] The inequalities are seen in virtually all indicators of health. In the Netherlands, for instance, social disadvantage is associated with a life expectancy reduction between 6 to 7 years and with a reduction in healthy (without disability) life years of 16 to 19 years.[5] This is the consequence of higher rates of different diseases among socially disadvantaged persons, such as cardiovascular disease[6 7], cancer[8], and psychiatric disorders[9 10], like depression, anxiety disorders, and schizophrenia. Analogous to the social disadvantage gradient in morbidity and mortality in adult life, health inequalities are also frequently observed in children and adolescents. Higher rates of obesity[11], asthma[12 13], and infectious diseases[14 15] as well as a smaller attained length[13 16-18] among children from socially disadvantaged backgrounds have been reported. Furthermore, inequalities in behaviour and cognition during childhood are also often observed. Adolescents and school aged children growing up in socially disadvantaged families display more behavioural problems and are more often diagnosed with psychiatric disorders, such as disruptive behavioural disorders, ADHD, and depression.[19-34] Frequently, socially disadvantaged children show delays in different developmental areas, such as language and motor development as well as general cognitive function.[35-39] Given this, it is not surprising that these children tend to perform less well in schools and have a lower educational attainment.[40 41] A social disadvantage gradient has also been found in pregnancy and birth outcomes: women with a low socio-economic or ethnic minority background have higher risks of pregnancy complications and adverse birth outcomes such as pre-eclampsia[42 43], preterm birth[44-49], and low birth weight[49-54 55-57]. The neonatal morbidity and mortality rates are also higher in socially disadvantaged families.[58-60]

To summarize, health inequalities between socially advantaged and disadvantaged people are widespread and seem to involve the whole spectrum of health and disease. Obviously, prevention of these undesirable health inequalities is a major public health goal. Health inequalities between socially advantaged and disadvantaged people are already present early in life and persevere throughout the whole life span. Consequently, attempts to tackle this gradient in health should start by reducing socio-economic and ethnic inequalities in fetal life and infancy. However, the indicators of social disadvantage, such as low socio-economic status and ethnic minority status, are not easily amendable. Therefore, it is necessary

to unravel the pathways through which social disadvantage leads to health and disease. These pathways might offer a window of opportunity for prevention and intervention programs.

As mentioned above, the relation between social disadvantage and health is probably not a direct one: the effect of social disadvantage on health is likely to act trough a number of more specific health determinants that are unequally distributed across different socio-economic and ethnic groups. Research has started to evaluate the pathways through which social disadvantage influences health.[61 62]

Regarding birth outcomes, different indicators of socio-economic status have frequently been associated with higher rates of preterm birth[44-49] and low birth weight[49-57]. A younger age, shorter height and smoking habits of women with a low socio-economic status explained a small part of these elevated risks.[44-46 55-57] It has been hypothesized that psychosocial risk factors and unhealthy lifestyle habits explain part of the inequalities in pregnancy outcomes, as these factors are both more prevalent among women in socially disadvantaged groups and are determinants of pregnancy outcomes like preterm birth and birth weight.[63 64] These hypotheses have not yet been verified.

Even though there is extensive literature on socioeconomic inequalities in behavioural problems[19-29], few studies have been carried out on the association between socioeconomic status and infant temperament[65-68], which is a way to conceptualise early emotional differences. Likewise, the indications of behavioural and mental health problems among ethnic minority children stem from studies among school-aged children and adolescents[30-34], while research hardly focussed on preschool children. Recent research identified young parental age and single parenthood as explanatory factors in the association between social disadvantage and behaviour.[19 29] However, many other factors might be involved and explain differences in mental health. Indicators of parental psychosocial well being are associated with child behavioural problems.[23 69-71] One can think of parental psychopathology, parents knowledge about and skills in caretaking practices, financial strain, and family stress, just to name a few. As psychosocial functioning of persons is also related to their social position, these variables might be on the pathway between social disadvantage and child behaviour.

In conclusion, the exact pathways how social disadvantage 'gets under the skin' and causes poor health are only partially known. Therefore, this thesis aimed to extend the existing knowledge on the relation between social disadvantage and health and behaviour early in life. The studies were conducted in The Generation R Study, which offers a unique opportunity to investigate whether biological and environmental factors during pregnancy and the first years of life can explain social inequalities in infant health and behaviour.

The specific aims of this thesis were:

1a. To study the association between social disadvantage and pregnancy outcomes, of which preterm birth and birth weight were the main focus.

1b. To examine explanatory mechanisms in educational and employment-related inequalities in adverse pregnancy outcomes.

2a. To study the association of social disadvantage with child behaviour and parental harsh discipline in early childhood.

2b. To examine explanatory mechanisms in socioeconomic and ethnic inequalities in child behaviour and parental harsh discipline.

The Generation R Study is a prospective population-based cohort study from fetal life onwards in Rotterdam, the Netherlands.[72-75] Generation R is designed to identify early environmental and biological determinants of growth, development and health in fetal life and childhood. The socioeconomically diverse and multi-ethnic character of this urban cohort makes it an ideal setting to study the aims of this thesis.

Briefly, all pregnant women living in the study area with a delivery date between April 2002 and January 2006 were eligible for enrolment in the Generation R Study. Health care workers like community midwives and obstetricians informed pregnant women about the study. Enrolment was aimed early during pregnancy, but was possible until birth of the child. During pregnancy, assessments included questionnaires, physical examinations of the women and their partners, and fetal ultrasound examinations. The questionnaires assessed a wide range of topics regarding health related issues, psychosocial functioning and life style habits of the participants. Assessments were planned in early pregnancy (<18 weeks' gestation), mid-pregnancy (18-25 weeks' gestation) and late pregnancy (≥25 weeks' gestation). Information on pregnancy complications, birth outcomes, and indicators of neonatal health was obtained from the medical records of the hospital and midwife registries. After birth, assessments carried on through routine visits to child health centers and by means of questionnaires at 2, 6, 12, 18, 24, 30, and 36 months. In these questionnaires, parents reported repeatedly on their child's health, development, and behaviour. Several times, they were also asked to report on their own health and parenting style.

In total, 9778 pregnant women were included, of whom 8880 enrolled in the prenatal part of the study. The participating women gave birth to 9745 live born children. Due to exclusion of participants from the pilot phase (12%) and because of withdrawal from the study (7%), 7893 children participated in the postnatal phase of the Generation R Study. Of 598 children, parents gave solely permission to use information obtained from the child health centers. Full consent for the postnatal phase of the Generation R Study, which included obtaining information from the child health centers as well as assessments via postal questionnaires, was obtained from 7295 children and their parents. Due to missing data on determinants or

outcomes and because of specific exclusion criteria, the population for analysis differed between the various studies presented in this thesis.

OUTLINE

In chapter 2, the association between social disadvantage and different pregnancy outcomes is studied. Educational differences in fetal growth (chapter 2.1), preterm birth (chapter 2.2), and birth weight (chapter 2.3) are presented with a focus on the mediating mechanisms that possibly explain the associations. Furthermore, the association between (un)employment and maternal pregnancy complications, delivery outcomes and markers of neonatal health are studied (chapter 2.4). Chapter 3 shows the relation between social disadvantage and behaviour of both children and their parents during early childhood. Socioeconomic inequalities in infant temperament and ethnic differences in behavioural problems of toddlers are presented (chapters 3.1 and 3.2). In both studies, the role of family risk factors is explored as possible explanatory mechanisms. With regard to the ethnic differences in child behaviour, we additionally examined the role of immigration characteristics of the mothers. In chapter 3.3 sociodemographic and psychosocial determinants of use of harsh discipline by mothers and fathers are studied, as harsh discipline presents a risk for healthy child development. Finally, the main findings of this thesis are interpreted and some methodological aspects of the studies are discussed (chapter 4). Additionally, implications for future research as well as suggestions for public health and clinical practice are presented.

REFERENCES

1. Berkman LF, Kawachi I. *Social Epidemiology*. New York, USA: Oxford University Press, Inc., 2000.
2. Mackenbach JP, Kunst AE, Cavelaars AE, Groenhof F, Geurts JJ. Socioeconomic inequalities in morbidity and mortality in western Europe. The EU Working Group on Socioeconomic Inequalities in Health. *Lancet* 1997;349(9066):1655-9.
3. Mackenbach JP, Stirbu I, Roskam AJ, Schaap MM, Menvielle G, Leinsalu M, et al. Socioeconomic inequalities in health in 22 European countries. *N Engl J Med* 2008;358(23):2468-81.
4. Poulton R, Caspi A, Milne BJ, Thomson WM, Taylor A, Sears MR, et al. Association between children's experience of socioeconomic disadvantage and adult health: a life-course study. *Lancet* 2002;360(9346):1640-5.
5. Statistiek CBvd. *Gezondheid en zorg in cijfers 2008*. Den Haag: Centraal Bureau voor de Statistiek, 2008.
6. Kaplan GA, Keil JE. Socioeconomic factors and cardiovascular disease: a review of the literature. *Circulation* 1993;88(4 Pt 1):1973-98.
7. Mackenbach JP, Cavelaars AE, Kunst AE, Groenhof F. Socioeconomic inequalities in cardiovascular disease mortality; an international study. *Eur Heart J* 2000;21(14):1141-51.
8. Ward E, Jemal A, Cokkinides V, Singh GK, Cardinez C, Ghafoor A, et al. Cancer disparities by race/ethnicity and socioeconomic status. *CA Cancer J Clin* 2004;54(2):78-93.
9. Carta MG, Bernal M, Hardoy MC, Haro-Abad JM, Report on the Mental Health in Europe Working Group. Migration and mental health in Europe (the state of the mental health in Europe working group: appendix 1). *Clin Pract Epidemol Ment Health* 2005;1:13.
10. Henderson C, Thornicroft G, Glover G. Inequalities in mental health. *Br J Psychiatry* 1998;173:105-9.
11. Wang Y, Beydoun MA. The obesity epidemic in the United States--gender, age, socioeconomic, racial/ethnic, and geographic characteristics: a systematic review and meta-regression analysis. *Epidemiol Rev* 2007;29:6-28.
12. Smith LA, Hatcher-Ross JL, Wertheimer R, Kahn RS. Rethinking race/ethnicity, income, and childhood asthma: racial/ethnic disparities concentrated among the very poor. *Public Health Rep* 2005;120(2):109-16.
13. Seguin L, Xu Q, Gauvin L, Zunzunegui MV, Potvin L, Frohlich KL. Understanding the dimensions of socioeconomic status that influence toddlers' health: unique impact of lack of money for basic needs in Quebec's birth cohort. *J Epidemiol Community Health* 2005;59(1):42-8.
14. Paradise JL, Rockette HE, Colborn DK, Bernard BS, Smith CG, Kurs-Lasky M, et al. Otitis media in 2253 Pittsburgh-area infants: prevalence and risk factors during the first two years of life. *Pediatrics* 1997;99(3):318-33.
15. Thrane N, Sondergaard C, Schonheyder HC, Sorensen HT. Socioeconomic factors and risk of hospitalization with infectious diseases in 0- to 2-year-old Danish children. *Eur J Epidemiol* 2005;20(5):467-74.
16. Herngreen WP, van Buuren S, van Wieringen JC, Reerink JD, Verloove-Vanhorick SP, Ruys JH. Growth in length and weight from birth to 2 years of a representative sample of Netherlands children (born in 1988-89) related to socioeconomic status and other background characteristics. *Ann Hum Biol* 1994;21(5):449-63.

17. du Prel X, Kramer U, Behrendt H, Ring J, Oppermann H, Schikowski T, et al. Preschool children's health and its association with parental education and individual living conditions in East and West Germany. *BMC Public Health* 2006;6:312.
18. Whincup PH, Cook DG, Shaper AG. Social class and height. *Bmj* 1988;297(6654):980-1.
19. Bradley RH, Corwyn RF. Socioeconomic status and child development. *Annu Rev Psychol.* 2002;53:371-99.
20. Ford T, Goodman R, Meltzer H. The relative importance of child, family, school and neighbourhood correlates of childhood psychiatric disorder. *Soc Psychiatry Psychiatr Epidemiol* 2004;39(6):487-96.
21. Johnson JG, Cohen P, Dohrenwend BP, Link BG, Brook JS. A longitudinal investigation of social causation and social selection processes involved in the association between socioeconomic status and psychiatric disorders. *J Abnorm Psychol.* 1999;108(3):490-9.
22. Scahill L, Schwab-Stone M, Merikangas KR, Leckman JF, Zhang H, Kasl S. Psychosocial and clinical correlates of ADHD in a community sample of school-age children. *J Am Acad Child Adolesc Psychiatry* 1999;38(8):976-84.
23. Campbell SB. Behavior problems in preschool children: a review of recent research. *J Child Psychol Psychiatry.* 1995;36(1):113-49.
24. Caspi A, Taylor A, Moffitt TE, Plomin R. Neighborhood deprivation affects children's mental health: environmental risks identified in a genetic design. *Psychol Sci.* 2000;11(4):338-42.
25. Kahn RS, Wilson K, Wise PH. Intergenerational health disparities: socioeconomic status, women's health conditions, and child behavior problems. *Public Health Rep.* 2005;120(4):399-408.
26. Kalff AC, Kroes M, Vles JS, Hendriksen JG, Feron FJ, Steyaert J, et al. Neighbourhood level and individual level SES effects on child problem behaviour: a multilevel analysis. *J Epidemiol Community Health.* 2001;55(4):246-50.
27. Maughan B, Collishaw S, Meltzer H, Goodman R. Recent trends in UK child and adolescent mental health. *Soc Psychiatry Psychiatr Epidemiol* 2008;43(4):305-10.
28. Reijneveld SA, Brugman E, Verhulst FC, Verloove-Vanhorick SP. Area deprivation and child psychosocial problems--a national cross-sectional study among school-aged children. *Soc Psychiatry Psychiatr Epidemiol.* 2005;40(1):18-23.
29. Kalff AC, Kroes M, Vles JS, Bosma H, Feron FJ, Hendriksen JG, et al. Factors affecting the relation between parental education as well as occupation and problem behaviour in Dutch 5- to 6-year-old children. *Soc Psychiatry Psychiatr Epidemiol* 2001;36(7):324-31.
30. Stevens GW, Vollebergh WA. Mental health in migrant children. *J Child Psychol Psychiatry* 2008;49(3):276-294.
31. Reijneveld SA, Harland P, Brugman E, Verhulst FC, Verloove-Vanhorick SP. Psychosocial problems among immigrant and non-immigrant children--ethnicity plays a role in their occurrence and identification. *Eur Child Adolesc Psychiatry* 2005;14(3):145-52.
32. Bengi-Arslan L, Verhulst FC, van der Ende J, Erol N. Understanding childhood (problem) behaviors from a cultural perspective: comparison of problem behaviors and competencies in Turkish immigrant, Turkish and Dutch children. *Soc Psychiatry Psychiatr Epidemiol* 1997;32(8):477-84.

33. Gross D, Fogg L, Young M, Ridge A, Cowell JM, Richardson R, et al. The equivalence of the Child Behavior Checklist/1 1/2-5 across parent race/ethnicity, income level, and language. *Psychol Assess* 2006;18(3):313-23.
34. Vollebergh WA, ten Have M, Dekovic M, Oosterwegel A, Pels T, Veenstra R, et al. Mental health in immigrant children in the Netherlands. *Soc Psychiatry Psychiatr Epidemiol* 2005;40(6):489-96.
35. Brooks-Gunn J, Klebanov PK, Duncan GJ. Ethnic differences in children's intelligence test scores: role of economic deprivation, home environment, and maternal characteristics. *Child Dev.* 1996;67(2):396-408.
36. Hoff E. The specificity of environmental influence: socioeconomic status affects early vocabulary development via maternal speech. *Child Dev.* 2003;74(5):1368-78.
37. Raviv T, Kessenich M, Morrison FJ. A mediational model of the association between socioeconomic status and three-year-old language abilities: The role of parenting factors. *Early Childhood Research Quarterly.*;19(4):528-547.
38. Najman JM, Aird R, Bor W, O'Callaghan M, Williams GM, Shuttlewood GJ. The generational transmission of socioeconomic inequalities in child cognitive development and emotional health. *Soc Sci Med.* 2004;58(6):1147-58.
39. Kelly Y, Sacker A, Schoon I, Nazroo J. Ethnic differences in achievement of developmental milestones by 9 months of age: The Millennium Cohort Study. *Dev Med Child Neurol* 2006;48(10):825-30.
40. Haveman R, Wolfe B. The determinants of children's attainments. *J Economic Lit* 1995;33:1829-1878.
41. Blanden J, Gregg P. Family income and educational attainment: A review of approaches and evidence for Britain. *Oxford Rev Economic Policy* 2004;20(2):245-263.
42. Clausen T, Oyen N, Henriksen T. Pregnancy complications by overweight and residential area. A prospective study of an urban Norwegian cohort. *Acta Obstet Gynecol Scand* 2006;85(5):526-33.
43. Haelterman E, Qvist R, Barlow P, Alexander S. Social deprivation and poor access to care as risk factors for severe pre-eclampsia. *Eur J Obstet Gynecol Reprod Biol* 2003;111(1):25-32.
44. Ancel PY, Saurel-Cubizolles MJ, Di Renzo GC, Papiernik E, Breart G. Social differences of very preterm birth in Europe: interaction with obstetric history. Europop Group. *Am J Epidemiol* 1999;149(10):908-15.
45. Gissler M, Merilainen J, Vuori E, Hemminki E. Register based monitoring shows decreasing socioeconomic differences in Finnish perinatal health. *J Epidemiol Community Health.* 2003;57(6):433-9.
46. Luo ZC, Wilkins R, Kramer MS. , Fetal and Infant Health Study Group of the Canadian Perinatal Surveillance System. Effect of neighbourhood income and maternal education on birth outcomes: a population-based study. *CMAJ* 2006;174(10):1415-20.
47. Peacock JL, Bland JM, Anderson HR. Preterm delivery: effects of socioeconomic factors, psychological stress, smoking, alcohol, and caffeine. *BMJ.* 1995;311(7004):531-5.
48. Smith LK, Draper ES, Manktelow BN, Dorling JS, Field DJ. Socioeconomic inequalities in very preterm birth rates. *Arch Dis Child Fetal Neonatal Ed* 2007;92(1):F11-4.
49. Migone A, Emanuel I, Mueller B, Daling J, Little RE. Gestational duration and birthweight in white, black and mixed-race babies. *Paediatr Perinat Epidemiol* 1991;5(4):378-91.

50. Koupilova I, Bobak M, Holcik J, Pikhart H, Leon DA. Increasing social variation in birth outcomes in the Czech Republic after 1989. *Am J Public Health.* 1998;88(9):1343-7.
51. Luo ZC, Kierans WJ, Wilkins R, Liston RM, Mohamed J, Kramer MS. Disparities in birth outcomes by neighborhood income: temporal trends in rural and urban areas, british columbia. *Epidemiol.* 2004;15(6):679-86.
52. Mackenbach JP. Socio-economic health differences in The Netherlands: a review of recent empirical findings. *Soc Sci Med.* 1992;34(3):213-26.
53. Moser K, Li L, Power C. Social inequalities in low birth weight in England and Wales: trends and implications for future population health. *J Epidemiol Community Health.* 2003;57(9):687-91.
54. David RJ, Collins JW, Jr. Differing birth weight among infants of U.S.-born blacks, African-born blacks, and U.S.-born whites. *N Engl J Med* 1997;337(17):1209-14.
55. Koupilova I, Rahu K, Rahu M, Karro H, Leon DA. Social determinants of birthweight and length of gestation in Estonia during the transition to democracy. *Int J Epidemiol.* 2000;29(1):118-24.
56. Raum E, Arabin B, Schlaud M, Walter U, Schwartz FW. The impact of maternal education on intrauterine growth: a comparison of former West and East Germany. *Int J Epidemiol.* 2001;30(1):81-7.
57. Reime B, Ratner PA, Tomaselli-Reime SN, Kelly A, Schuecking BA, Wenzlaff P. The role of mediating factors in the association between social deprivation and low birth weight in Germany. *Soc Sci Med.* 2006;62(7):1731-44.
58. Alexander GR, Kogan M, Bader D, Carlo W, Allen M, Mor J. US birth weight/gestational age-specific neonatal mortality: 1995-1997 rates for whites, hispanics, and blacks. *Pediatrics.* 2003;111(1):e61-6.
59. Din-Dzietham R, Hertz-Picciotto I. Infant mortality differences between whites and African Americans: the effect of maternal education. *Am J Public Health* 1998;88(4):651-6.
60. Whitehead M, Drever F. Narrowing social inequalities in health? analysis of trends in mortality among babies of lone mothers (abridged version 2). *Bmj* 1999;318(7188):912-4.
61. Mackenbach JP, Howden-Chapman P. New perspectives on socioeconomic inequalities in health. *Perspect Biol Med* 2003;46(3):428-44.
62. Marmot M. Social determinants of health inequalities. *Lancet* 2005;365(9464):1099-104.
63. Kramer MS, Seguin L, Lydon J, Goulet L. Socio-economic disparities in pregnancy outcome: why do the poor fare so poorly? *Paediatr Perinat Epidemiol.* 2000;14(3):194-210.
64. Moutquin JM. Socio-economic and psychosocial factors in the management and prevention of preterm labour. *BJOG.* 2003;110 Suppl 20:56-60.
65. Matheny AP, Wilson RS, Thoben AS. Home and Mother: Relations with Infant Temperament. *Dev Psychol.* 1987;23(3):323-331.
66. Maziade M. Infant temperament: SES and Gender Differences and Reliability of Measurement in a Large Quebec Sample. *Merrill-Palmer Quarterly.* 1984;30(2):213-26.
67. Persson-Blennow I, McNeil TF. Temperament characteristics of children in relation to gender, birth order, and social class. *Am J Orthopsychiatry.* 1981;51(4):710-4.
68. Sameroff AJ, Seifer R, Elias PK. Sociocultural variability in infant temperament ratings. *Child Dev* 1982;53(1):164-73.

69. Rutter M, Yule B, Quinton D, Rowlands O, Yule W, Berger M. Attainment and adjustment in two geographical areas: III–Some factors accounting for area differences. *Br J Psychiatry* 1975;126:520-33.
70. Eskenazi B, Castorina R. Association of prenatal maternal or postnatal child environmental tobacco smoke exposure and neurodevelopmental and behavioral problems in children. *Environ Health Perspect* 1999;107(12):991-1000.
71. Linnet KM, Dalsgaard S, Obel C, Wisborg K, Henriksen TB, Rodriguez A, et al. Maternal lifestyle factors in pregnancy risk of attention deficit hyperactivity disorder and associated behaviors: review of the current evidence. *Am J Psychiatry* 2003;160(6):1028-40.
72. Hofman A, Jaddoe VW, Mackenbach JP, Moll HA, Snijders RF, Steegers EA, et al. Growth, development and health from early fetal life until young adulthood: the Generation R Study. *Paediatr Perinat Epidemiol.* 2004;18(1):61-72.
73. Jaddoe VW, Bakker R, van Duijn CM, van der Heijden AJ, Lindemans J, Mackenbach JP, et al. The Generation R Study Biobank: a resource for epidemiological studies in children and their parents. *Eur J Epidemiol* 2007;22(12):917-23.
74. Jaddoe VW, Mackenbach JP, Moll HA, Steegers EA, Tiemeier H, Verhulst FC, et al. The Generation R Study: Design and cohort profile. *Eur J Epidemiol.* 2006;21(6):475-84.
75. Jaddoe VW, van Duijn CM, van der Heijden AJ, Mackenbach JP, Moll HA, Steegers EA, et al. The Generation R Study: design and cohort update until the age of 4 years. *Eur J Epidemiol* 2008.

CHAPTER 2

SOCIAL DISADVANTAGE AND PREGNANCY OUTCOMES

CHAPTER **2.1**

Mother's educational level and fetal growth; the genesis of health inequalities

ABSTRACT

OBJECTIVES: To study level of maternal education (high, mid-high, mid-low and low) and its association with fetal weight, head circumference, abdominal circumference, and femur length, measured in different periods of pregnancy. Main hypotheses: low maternal education is associated with a slower fetal growth and equally affects different parts of the fetal body.

DESIGN: Population-based prospective cohort study (The Generation R Study).

SETTING AND PARTICIPANTS: Pregnant women living in Rotterdam, the Netherlands, who gave birth between April 2002 and January 2006. Analyses were restricted to 3545 pregnant women with a Dutch ethnicity and available data.

MAIN OUTCOME MEASURES: Fetal weight, head circumference, abdominal circumference and femur length, measured with ultrasound in mid and late pregnancy.

RESULTS: In fetuses of women with low education relative to those of women with high education, fetal growth was slower, leading to a lower fetal weight that was statistically significant from late pregnancy onwards. In these fetuses, growth of the head (-0.16 mm/week; 95% CI: -0.25 to 0.07), abdomen (-0.10 mm/week; 95% CI: -0.21 to 0.01) and femur (-0.03 mm/week; 95% CI: -0.05 to 0.005) were all slower; from mid-pregnancy onwards, head circumference was significantly smaller, and from late pregnancy onwards, femur length was also significantly smaller. The negative effect of low education was greatest for head circumference (difference in standard-deviation score in late pregnancy: -0.26; 95% CI: -0.36 to 0.16). This effect remained statistically significant even after adjustment for various potential mediators (adjusted difference: -0.14; 95% CI: -0.25 to 0.03).

CONCLUSION: Low maternal education impairs fetal growth and appears to affect growth of the fetal brain more than that of peripheral and abdominal tissues. This might have consequences for later cognitive ability, educational attainment and job performance for the offspring of low-educated mothers.

INTRODUCTION

Fetal growth is an important determinant of future health.[1-5] An impaired fetal growth increases the risk of perinatal and neonatal death[1], and of various medical and developmental problems in childhood[3 4 6]. Furthermore, there is accumulating evidence that poor fetal growth is associated with chronic diseases in adult life, particularly cardiovascular diseases.[2 5]

Fetal growth is determined by a complex interplay of genetic and environmental factors.[7] One important environmental factor is socioeconomic status, as indicated by educational level, income level or occupation. Compared with women of high socioeconomic status, those of low socioeconomic status give birth to babies with a lower birth weight.[8 9] These socioeconomic inequalities in birth weight suggest that factors related to a low socioeconomic status of the mother impair fetal growth.[9] Until now, only one study actually related socioeconomic status to direct measures of fetal growth rather than size at birth.[10] However, the authors used an area-based index of socioeconomic status rather than an individual-based measure, and studied fetal-growth characteristics measured only in mid pregnancy, which limited the possibility to assess fetal-growth patterns. Because prospective population-based studies on the effect of maternal socioeconomic status on fetal growth trajectories are lacking, it is not known whether 1) socioeconomic differences in fetal growth are constant over time, 2) from which moment onwards differences in fetal size become apparent, and 3) whether low socioeconomic status equally affects different parts of the fetal body.

Therefore, among pregnant women participating in a population-based cohort study, we studied level of maternal education as an indicator of socioeconomic status and its association with fetal weight, head circumference, abdominal circumference, and femur length, measured in different periods of pregnancy. Assuming that a low maternal education is associated with a slower fetal growth, we expected that educational differences in fetal size can be observed from late pregnancy onwards, since in that period inter-individual variability in fetal size is highest.[11] Because available data suggest that socioeconomic status does not affect proportionality at birth,[12] we hypothesized head circumference, abdominal circumference, and femur length to be equally affected by low maternal education.

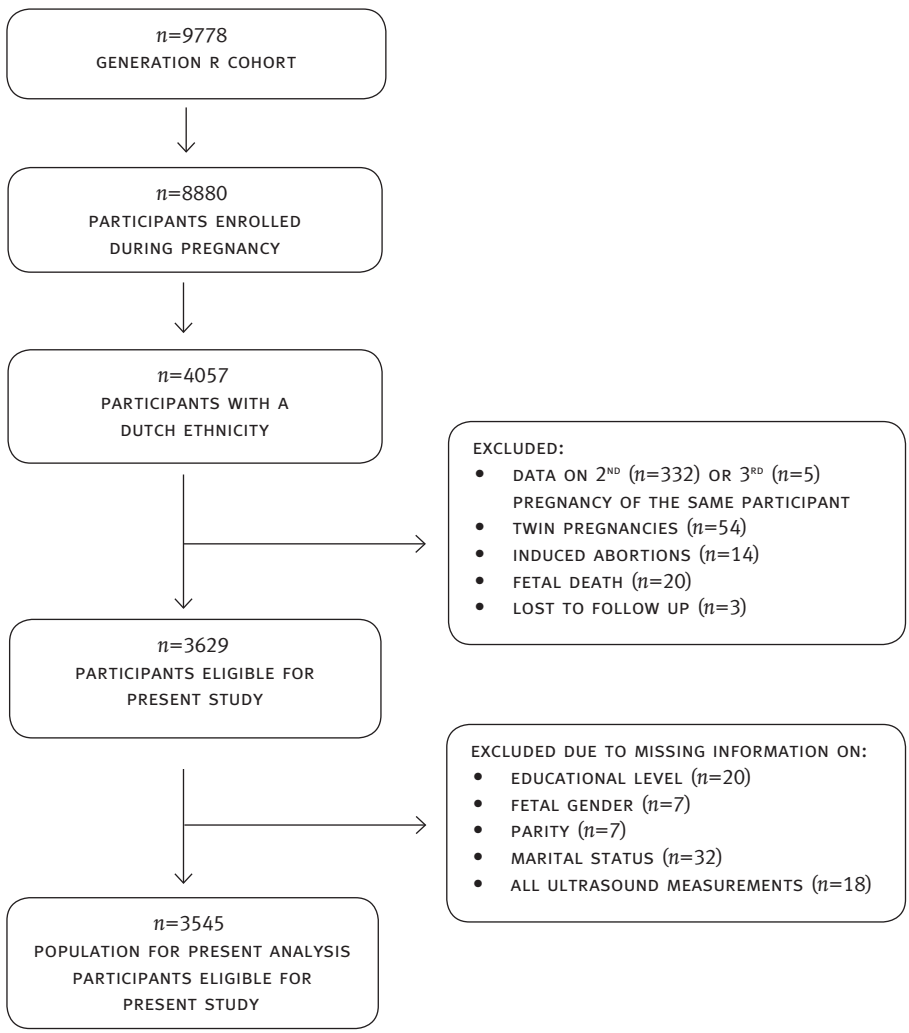
METHODS

THE GENERATION R STUDY

The present study was embedded within the Generation R Study, a population-based prospective cohort study from fetal life until young adulthood. The Generation R Study has previously been described in detail.[13] Briefly, all mothers with an expected delivery date between April 2002 and January 2006 and living in Rotterdam, the Netherlands, were eligible for participation in the study. While enrolment ideally took place in early pregnancy, it was possible until after the birth of the child. In

total, 9778 mothers of various ethnicities and their children were included and followed-up (participation rate 61%).[13] Assessments during pregnancy took place in early pregnancy (gestational age <18 weeks), mid pregnancy (gestational age 18-25 weeks) and late pregnancy (gestational age ≥25 weeks). The study was conducted in accordance with the guidelines proposed in the World Medical Association Declaration of Helsinki, and has been approved by the Medical Ethical Committee at the Erasmus University Medical Center Rotterdam. Written consent was obtained from all participating parents.

FIGURE 1. FLOW CHART PARTICIPANTS



STUDY POPULATION

Of the 9778 women, 91% (n=8880) were enrolled during pregnancy.[13] Because educational inequalities in pregnancy outcome may differ between ethnic groups.[14] We restricted the present analyses to women with a Dutch ethnicity (n=4057). A woman was classified as Dutch if she reported that both her parents had been born in the Netherlands.[15] For several reasons, 512 women were excluded from analysis (figure 1), leaving a study population of 3545 women.

EDUCATIONAL LEVEL

At enrolment, we used a questionnaire to establish the highest education achieved by each mother. This was categorized into four levels:

1. high (university degree)
2. mid-high (higher vocational training)
3. mid-low (>3 years general secondary school, intermediate vocational training)
4. low (no education, primary school, lower vocational training, intermediate general school, or ≤3 years at general secondary school).[16]

FETAL ULTRASOUND MEASUREMENTS AND BIRTH WEIGHT

Trained sonographers carried out fetal ultrasound measurements in early, mid and late pregnancy, which were used to establish gestational age and to measure fetal-growth characteristics.[17] For the analyses presented below, we used the measurements in mid and late pregnancy of head circumference, abdominal circumference and femur length, as measurements in early pregnancy were intended primarily for pregnancy dating. All growth characteristics were measured to the nearest millimetre using standardized procedures.[18] The estimated fetal weight was calculated on the basis of head circumference, abdominal circumference and femur length.[19] For the models for estimated fetal weight, we also used information on birth weight and gestational age at birth, which was obtained from midwife and hospital registries. Longitudinal growth curves and gestational-age adjusted standard-deviation (SD) scores were constructed for all growth measurements.[17]

COVARIATES

Any effect of educational level on fetal growth is probably an indirect one, acting through other more proximal determinants of fetal growth, so-called mediators.[20] The factors listed below were included in this study as potential mediators, because these factors have been shown to contribute significantly to explaining socio-economic inequalities in size at birth.[8]

Maternal anthropometrics

Maternal height was measured in the research centers. Pre-pregnancy weight was established at enrolment through questionnaire. On the basis of height and pre-pregnancy weight (weight/height^2) we calculated pre-pregnancy body mass index (BMI).

Smoking
Through questionnaires in early, mid and late pregnancy, we obtained information on smoking during pregnancy (no, until pregnancy was known, continued in pregnancy).

Psychosocial and material factors
Using questionnaires during pregnancy we established marital status (married/cohabiting, single motherhood), whether the pregnancy was planned (yes, no), and the presence of financial difficulties (yes, no).

All models were adjusted for fetal gender, and maternal age and parity. As we did fetal gender, we treated maternal age and parity as potential confounders, since they cannot be considered indisputable mediators.[20] Information on fetal gender was obtained from midwife and hospital registries. Maternal age was established at enrolment in the study. Parity, which in this study was defined as the number of previous live births (0, ≥1), was obtained through a questionnaire at enrolment.

STATISTICAL ANALYSES
We started by evaluating the effect of educational level on overall fetal growth, after which we separately analysed the associations of educational level with head circumference, abdominal circumference and femur length. These associations were examined using longitudinal multilevel analysis, as this type of analysis takes account of the correlation between repeated measures on the same subject and allows for incomplete outcome data.[21] The best fitting model to predict each growth characteristic as a function of gestational age was built using fractional polynomials.[22] To these models we added educational level as a main determinant (reference: high education), and an interaction term of educational level with gestational age. The best-fitting model structures are presented in APPENDIX 1. These models were based on 10387 observations for fetal weight and birth weight, 6845 for head circumference, 6876 for abdominal circumference, and 6882 for femur length.

Using the same strategy, additional models were constructed for the SD scores for each growth characteristic (APPENDIX 1). To evaluate educational differences in fetal size, SD scores were compared between educational subgroups at specific timepoints in pregnancy, i.e. at 20, 30 and 40 weeks for estimated fetal weight, and at 20 and 30 weeks for head circumference, abdominal circumference, femur length. For each growth characteristic, we started with a model that included the confounders (basic model). Next, this model was additionally adjusted for the potential mediators (fully adjusted model) to establish to what extent educational differences in fetal growth or size could be explained by these factors.

For each covariate, an interaction term with gestational age was tested for significance. If the test was significant, these interactions were retained in the model. A p-value of 0.05 was taken to indicate statistical significance; for interaction terms we used a p-value of 0.10. Because additional interaction terms between educational level and covariate*gestational age would lead to difficult to interpret results,

these were not included in the models.

To handle missing values in the covariates (all ≤13%, see table 1) we applied multiple imputation based on five imputed data sets ('PROC MI' procedure in SAS 9.1.3).[23] Imputations were based on the relationships between all covariates included in this study. Statistical analyses were performed using Statistical Package of Social Sciences version 15.0 for Windows (SPSS Inc, Chicago, IL, USA) and the Statistical Analysis System (SAS) for Windows (SAS Institute Inc, USA), version 9.1.3.

RESULTS

TABLE 1 shows a description of the study population. Of the 3545 women in this study, 17.9% were in the lowest educational level and 31.3% in the highest. Compared with women with a high education, those with a low education were younger, shorter, heavier before pregnancy, less likely to be nulliparous, and gave birth to lighter babies; they were also more likely to smoke during pregnancy (p for trend for all <0.05). The mean values for the fetal-growth characteristics at the median gestational ages in mid and late pregnancy are presented in APPENDIX 2.

EDUCATIONAL LEVEL AND ESTIMATED FETAL WEIGHT

Relative to fetuses of women in the highest educational subgroup, those of women with mid-high, mid-low and low education had a slower fetal growth (FIGURE 2). Fetal growth rate was lowest in the fetuses of women with a low educational level, and the difference in fetal growth rate increased as pregnancy progressed. Women with a low educational level had significantly smaller fetuses from 30 weeks onwards (difference at 30 weeks: -0.16 SD; 95% CI: -0.25,-0.08; table 2). This difference became larger towards term (difference at 40 weeks: -0.35 SD; 95% CI: -0.46,-0.24). After adjustment for the potential mediators, the educational differences in estimated fetal weight attenuated, but at 40 weeks they remained statistically significant.

EDUCATIONAL LEVEL AND HEAD CIRCUMFERENCE, ABDOMINAL CIRCUMFERENCE AND FEMUR LENGTH

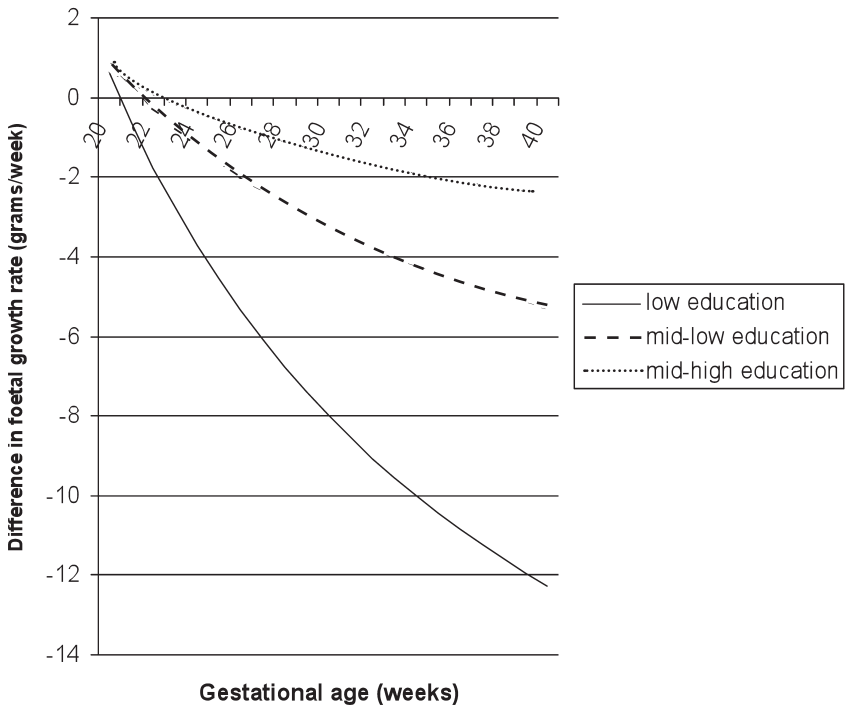
Educational level was associated with growth of the fetal head, abdomen and femur, with the slowest growth in the lowest educational subgroup (TABLE 3). Relative to fetuses of women with a high educational level, in fetuses of women with a low educational level growth of the head was on average 0.16 mm/week slower (95% CI: -0.25,-0.07), growth of the abdomen 0.10 mm/week slower (95% CI: -0.21, 0.01) and that of the femur 0.03 mm/week slower (95% CI: -0.05,-0.005). Adjustment for the potential mediators attenuated the difference in head growth and that in femur growth, but not the difference in abdominal growth. The largest attenuations were due to the adjustment for smoking, followed by maternal height (data not shown). The difference in head growth remained statistically significant after full adjustment.

TABLE 1. GENERAL CHARACTERISTICS IN THE TOTAL STUDY POPULATION AND BY MATERNAL EDUCATIONAL LEVEL (N=3545)[¶]

		MATERNAL EDUCATION				
	TOTAL (N=3545)	HIGH (N=1109)	MID-HIGH (N=877)	MID-LOW (N=925)	LOW (N=634)	P FOR TREND[#]
PREGNANCY CHARACTERISTICS						
Maternal age (years)	31.1 (4.6)	32.9 (3.2)	31.9 (3.8)	30.0 (4.8)	28.6 (5.6)	<0.001
Parity (% nullipara)	65.0	64.3	68.1	68.1	57.3	0.049
Infant gender (% girls)	49.6	49.6	49.6	50.7	47.8	0.706
Gestational age at birth (median in weeks, 95% range)	40.3 (35.7,42.4)	40.3 (35.9,42.4)	40.3 (36.3,42.4)	40.1 (35.9,42.3)	39.9 (34.3,42.3)	<0.001
Birth weight (grams)	3470.5 (561.6)	3538.6 (538.9)	3509.5 (547.8)	3448.5 (563.8)	3329.0 (589.3)	<0.001
MATERNAL ANTHROPOMETRICS						
Height (cm)	170.7 (6.4)	171.4 (6.0)	171.3 (6.3)	170.5 (6.4)	168.8 (6.7)	<0.001
Pre-pregnancy weight (kg)[$]	67.8 (12.4)	66.4 (9.7)	66.9 (11.3)	69.2 (13.3)	69.8 (15.9)	<0.001
Pre-pregnancy BMI (kg/m2)[$]	23.3 (4.0)	22.5 (2.9)	22.7 (3.5)	23.8 (4.4)	24.4 (5.3)	<0.001
PSYCHOSOCIAL AND MATERIAL FACTORS						
Pregnancy was planned						
No (%)	18.1	9.4	14.7	21.5	33.0	<0.001
Missing (%)	5.4	5.5	6.3	4.4	5.2	
Marital status (% single)	8.2	3.5	4.6	8.8	20.3	<0.001
Financial difficulties						
Yes (%)	10.7	4.1	8.3	12.5	22.7	<0.001
Missing (%)	11.8	5.9	5.8	13.4	27.9	
SMOKING						
No (%)	68.7	80.4	74.3	65.3	45.6	<0.001
Until pregnancy known (%)	8.0	7.8	9.0	8.8	6.0	
Continued during pregnancy (%)	17.3	5.1	10.7	20.1	43.5	
Missing (%)	6.0	6.7	5.9	5.8	4.9	

BMI: body mass index.
[¶] Values are means (with standard deviations) or medians (with 95% range) for continuous factors, or percentages for categorical factors.
[#] p-values are for chi-squared test for trend (categorical factors), and for (linear) trend component of one-way analysis of variance or kruskall-wallis test (continuous factors).
[$] Data on pre-pregnancy weight and pre-pregnancy BMI was missing in 13.2%.

FIGURE 2. ESTIMATED DIFFERENCES IN FETAL GROWTH RATE FOR FETUSES OF WOMEN WITH LOW, MID-LOW AND MID-HIGH EDUCATION RELATIVE TO FETUSES OF WOMEN WITH HIGH EDUCATION (N=3545)[¶]



*[¶] Values are based on multilevel models and represent the differences in fetal growth rate for fetuses of women with low, mid-low and mid-high education relative to those of women with high education. All values are adjusted for fetal gender, and maternal age and parity. The following covariate*gestational age interactions were also included: gender*gestational age, gender*ln(gestational age), age*gestational age, parity*gestational age.*

TABLE 2. ASSOCIATIONS BETWEEN MATERNAL EDUCATIONAL LEVEL AND STANDARD DEVIATION SCORES FOR ESTIMATED FETAL WEIGHT AT 20, 30 AND 40 WEEKS GESTATION (N=3545).

	Difference in standard deviation score (and 95% CI) for estimated fetal weight at 20 weeks gestation	
	Basic model¶	Fully adjusted#
Educational level		
High	Reference	Reference
Mid-high	0.02 (-0.07,0.11)	0.02 (-0.07,0.12)
Mid-low	0.08 (-0.01,0.17)	0.07 (-0.02,0.17)
Low	0.02 (-0.09,0.13)	0.05 (-0.07,0.17)
	Difference in standard deviation score (and 95% CI) for estimated fetal weight at 30 weeks gestation	
	Basic model¶	Fully adjusted#
Educational level		
High	Reference	Reference
Mid-high	-0.009 (-0.08,0.06)	0.002 (-0.07,0.07)
Mid-low	-0.03 (-0.10,0.05)	-0.01 (-0.09,0.06)
Low	**-0.16 (-0.25,-0.08)**	-0.07 (-0.16,0.02)
	Difference in standard deviation score (and 95% CI) for estimated birth weight at 40 weeks gestation	
	Basic model¶	Fully adjusted#
Educational level		
High	Reference	Reference
Mid-high	-0.04 (-0.13,0.05)	-0.02 (-0.11,0.06)
Mid-low	**-0.13 (-0.22,-0.04)**	**-0.10 (-0.19,-0.008)**
Low	**-0.35 (-0.46,-0.24)**	**-0.18 (-0.29,-0.07)**

*Values are based on multilevel models. CI: confidence interval. ¶Basic model: adjusted for fetal gender, and maternal age and parity. # Fully adjusted: adjusted for fetal gender, maternal age and parity, maternal height, pre-pregnancy BMI, smoking during pregnancy, single motherhood, whether the pregnancy was planned and financial difficulties. The following covariate*gestational age interactions were also included: gender*gestational age, gender*ln(gestational age), age*gestational age, parity*gestational age, height*gestational age, BMI* gestational age, smoking*gestational age, financial difficulties*gestational age.*

TABLE 3. ASSOCIATIONS BETWEEN MATERNAL EDUCATIONAL LEVEL AND GROWTH OF THE FETAL HEAD, ABDOMEN AND FEMUR (N=3545).

	Differences (and 95% CI) in fetal head circumference growth (mm/week)	
Educational level	Basic model¶	Fully adjusted#
High	Reference	Reference
Mid-high	-0.03 (-0.11,0.05)	-0.02 (-0.09,0.05)
Mid-low	**-0.09 (-0.17,-0.02)**	**-0.07 (-0.15,-0.001)**
Low	**-0.16 (-0.25,-0.07)**	**-0.10 (-0.19,-0.01)**
	Differences (and 95% CI) in fetal abdominal circumference growth (mm/week)	
Educational level	Basic model¶	Fully adjusted#
High	Reference	Reference
Mid-high	0.02 (-0.09,0.12)	0.02 (-0.08,0.12)
Mid-low	-0.01 (-0.11,0.09)	-0.04 (-0.14,0.07)
Low	-0.10 (-0.21,0.01)	-0.10 (-0.22,0.02)
	Differences (and 95% CI) in fetal femur length growth (mm/week)	
Educational level	Basic model¶	Fully adjusted#
High	Reference	Reference
Mid-high	-0.003 (-0.02,0.02)	0.001 (-0.02,0.02)
Mid-low	-0.01 (-0.03,0.004)	-0.003 (-0.02,0.01)
Low	**-0.03 (-0.05,-0.005)**	0.0005 (-0.02,0.02)

*Values are based on multilevel models. CI: confidence interval. ˚Basic model: adjusted for fetal gender, and maternal age and parity. #Fully adjusted: adjusted for fetal gender, maternal age and parity, maternal height, pre-pregnancy BMI, smoking during pregnancy, single motherhood, whether the pregnancy was planned and financial difficulties. The following covariate*gestational age interactions were also included: for head-circumference model: gender*gestational age, parity*gestational age, height*gestational age, BMI* gestational age, smoking*gestational age; for abdominal-circumference model: parity*gestational age, BMI* gestational age, smoking*gestational age; for femur-length model: gender*gestational age, parity*gestational age, height*gestational age, smoking*gestational age.*

TABLE 4. ASSOCIATIONS BETWEEN MATERNAL EDUCATIONAL LEVEL AND FETAL HEAD CIRCUMFERENCE, ABDOMINAL CIRCUMFERENCE AND FEMUR LENGTH (IN STANDARD DEVIATION SCORES) AT 20 AND 30 WEEKS GESTATION (N=3545).

	20 weeks gestation					
Educational level	HC (SD score) Basic model¶	HC (SD score) Fully adjusted#	AC (SD score) Basic model¶	AC (SD score) Fully adjusted#	FL (SD score) Basic model¶	FL (SD score) Fully adjusted#
High		Reference	Reference	Reference	Reference	Reference
Mid-high	-0.09 (-0.19,0.005)	-0.09 (-0.18,0.008)	0.005 (-0.09,0.10)	0.006 (-0.09,0.10)	0.01 (-0.08,0.11)	0.01 (-0.08,0.11)
Mid-low	-0.09 (-0.19,0.003)	-0.09 (-0.18,0.01)	-0.004 (-0.09,0.09)	0.002 (-0.09,0.10)	0.11 (0.02,0.21)	0.10 (0.004,0.19)
Low	-0.14 (-0.26,-0.03)	-0.10 (-0.22,0.03)	-0.03 (-0.14,0.08)	0.01 (-0.11,0.13)	0.03 (-0.08,0.13)	0.04 (-0.08,0.16)
	30 weeks gestation					
Educational level	HC (SD score) Basic model¶	HC (SD score) Fully adjusted#	AC (SD score) Basic model¶	AC (SD score) Fully adjusted#	FL (SD score) Basic model¶	FL (SD score) Fully adjusted#
High	Reference	Reference	Reference	Reference	Reference	Reference
Mid-high	-0.07 (-0.16,0.01)	-0.06 (-0.14,0.03)	0.02 (-0.07,0.11)	0.03 (-0.06,0.11)	-0.01 (-0.10,0.07)	-0.001 (-0.08,0.08)
Mid-low	-0.14 (-0.23,-0.06)	-0.11 (-0.20,-0.03)	0.001 (-0.09,0.09)	-0.006 (-0.10,0.08)	0.02 (-0.07,0.10)	0.04 (-0.04,0.13)
Low	-0.26 (-0.36,-0.16)	-0.14 (-0.25,-0.03)	-0.09 (-0.19,0.02)	-0.04 (-0.15,0.07)	-0.12 (-0.22,-0.02)	-0.006 (-0.11,0.10)

Values are based on multilevel models and represent differences in head circumference, abdominal circumference and femur length (expressed in standard-deviation scores) relative to fetuses of women with high educational level. HC: head circumference; AC: abdominal circumference; FL: femur length; SD-score: standard deviation score.
¶ Basic model: adjusted for fetal gender, and maternal age and parity.
 # Fully adjusted: adjusted for fetal gender, maternal age and parity, maternal height, pre-pregnancy BMI, smoking during pregnancy, single motherhood, whether the pregnancy was planned and financial difficulties.
*The following covariate*gestational age interactions were also included: for head-circumference model: gender*gestational age, parity*gestational age, height*gestational age, BMI* gestational age, smoking*gestational age; for abdominal-circumference model: parity*gestational age, BMI* gestational age, smoking*gestational age; for femur-length model: gender*gestational age, parity*gestational age, height*gestational age, smoking*gestational age.*

TABLE 4 presents the educational differences in size of the fetal head, abdomen and femur at 20 and 30 weeks gestation, expressed in SD-scores. Compared with fetuses of women with a high educational level, those of women with a low educational level had a significantly smaller head circumference from 20 weeks onwards; femur length was significantly smaller from 30 weeks onwards (basic models). Although abdominal circumference was also smaller in these fetuses, the difference did not reach statistical significance. The effect of low education was larger for head circumference than for femur length or abdominal circumference. After adjustment for the potential mediators, only the difference in SD score for head circumference at 30 weeks gestation remained significant.

DISCUSSION

The present study is the first to present a longitudinal assessment of the effect of an individual-level indicator of socioeconomic status on fetal growth. We demonstrated that a low maternal educational level is associated with a progressively slower fetal growth, causing differences in fetal weight that are statistically significant from late pregnancy onwards. This study also suggests that low maternal educational level predominantly affects growth of the fetal head, followed by growth of the fetal femur and abdomen.

METHODOLOGICAL CONSIDERATIONS

The main strength of this study lies in its population-based prospective design, with enrolment of a large number of women early in pregnancy, and extensive measurements during pregnancy.[13] Although there are other measures of socioeconomic status, including income level and occupational class,[24] we selected maternal educational level as a main indicator of socioeconomic status for two reasons: first educational level not only partly reflects material resources because it structures occupation and income, it also reflects non-economic social characteristics, such as general and health-related knowledge, literacy, problem-solving skills and prestige;[24,25] second, educational level has been shown to be the best socioeconomic predictor of pregnancy outcomes.[26] Furthermore, when we repeated the analyses using household income level as determinant, we found comparable results. There was one exception: income-related differences in fetal head circumference were statistically significant only from 30 weeks gestation onwards.

When interpreting the results of this study, one should take account of a number of limitations. First, our study was conducted in a Dutch, urban population, which limits generalizability of our results to non-Dutch or rural populations. Furthermore, although the participation rate was relatively high (61%, among Dutch women 68%)[13], there was some selection towards a study population that was relatively highly educated and more healthy.[27]

Second, while fetal ultrasound examinations are a more reliable basis than the last menstrual period for establishing gestational age,[28] it also has a disadvantage:

the growth variation before the first measurement of the fetal characteristics that were used for pregnancy dating, i.e. crown-rump length and biparietal diameter, was set to zero.[17] Since these characteristics are correlated throughout pregnancy with head circumference, abdominal circumference and femur length, our study may have underestimated the variation in the latter three growth characteristics, resulting in an underestimation of our effect estimates.

Finally, our study may have been vulnerable to misclassification, because many covariates were measured using questionnaires. In particular, smoking behaviour and pre-pregnancy weight may have been underreported. The effect on our results of this misclassification is difficult to predict, since we cannot be certain whether this misclassification was random or not.

MATERNAL EDUCATIONAL LEVEL AND FETAL GROWTH

The educational differences in fetal growth were large enough to result in apparent differences in fetal size already during pregnancy. As we hypothesized, differences in fetal weight were significant from late pregnancy onwards. In contrast with our expectations, however, the effect of low maternal education was not equal for the various body segments of the fetus. Relative to growth of the fetal femur and abdomen, the adverse effect of a low educational level seemed greatest for growth of the fetal head.

Clear educational differences in fetal head circumference were detectable already at 20 weeks gestation. By 30 weeks, significant educational differences in femur length could also be detected, but not in abdominal circumference, although there was a clear trend towards a smaller abdominal circumference in fetuses of lower educated women. The timing of the emergence of significant educational differences in head, femur and abdomen might be explained by the different growth patterns of the various fetal-growth components. Peak growth velocity for head circumference is steeper and occurs earlier (around 18 weeks) than that for femur length (around 20 weeks) and abdomen (around 22 weeks).[11 29]

Regarding the magnitude of the educational differences in size of the different body segments, one should take account of the timing of the ultrasound measurements. In our study, only 2.5% of these measurements took place after the 32nd week of gestation. For physiological pregnancies, it has been shown that the difference in abdominal circumference between smaller and larger babies increases with increasing gestational age.[29] Therefore, the observed educational differences in abdominal circumference might have been larger if we had had availability to more growth measurements near term. It is thus important that our results are confirmed in future studies with more comprehensive fetal-growth data and with information on proportionality at birth.

One possible explanation for a low maternal education being relatively more strongly associated with fetal head circumference is that the factors that mediate the effect of maternal education affect fetal head growth more than growth of the fetal femur and abdomen. In support of this explanation, we found the most important

mediators to be maternal smoking and maternal height. Maternal smoking during pregnancy, which was more prevalent among women with a low educational level than those with a high level, is known to cause fetal growth restriction including a smaller head circumference.[30] Maternal height, which was positively associated with educational level, has been found to be a significant determinant of disproportionality at birth; shorter mothers tend to give birth to babies that are shorter and have smaller heads for their weight,[12] which corresponds with the type of growth impairment associated with low maternal education. The potential mediators included in this study, however, explained only about half the educational differences in fetal head circumference at 30 weeks gestation. The remaining effect may be due to other factors, such as nutritional factors or genetic factors.[7 31] Since head circumference is associated with academic achievements[3 32] and maternal head circumference is a strong predictor of neonatal head circumference[33], there may be a common genetic link between head circumference of the mother, her educational achievement and head growth of her offspring. We had no information on head circumference of the mother. This merits further investigation.

In conclusion, this unique study demonstrates that a low socioeconomic status of the mother impairs fetal growth, and suggests that it affects growth of the fetal brain more than it affects peripheral and abdominal tissues. The socioeconomic inequalities in fetal growth as demonstrated here may represent the genesis of socioeconomic health inequalities in infancy, childhood and adulthood. In particular, since fetal head growth is associated with future cognitive functioning and academic achievement,[3 32] the observed socioeconomic inequalities in fetal head growth might have consequences for later cognitive ability, educational attainment and job performance for the offspring of low-educated mothers. Taking measures to narrow inequalities in fetal growth should be an important public health issue. Smoking during pregnancy being the most important modifiable factor explaining these inequalities, such measures should primarily be aimed at reducing smoking rates among pregnant women of low socioeconomic status. The use of a video in order to raise awareness of the consequences of smoking during pregnancy, a self-help manual and health counselling by midwives have been shown to be successful in helping pregnant women to stop smoking,[34] and should be applied more intensively to women with a low educational level. Further research is needed to provide other entry points for interventions and to study the short and long term consequences of socioeconomic inequalities in intra-uterine growth.

REFERENCES

1. Alexander GR, Kogan M, Bader D, Carlo W, Allen M, Mor J. US birth weight/gestational age-specific neonatal mortality: 1995-1997 rates for whites, hispanics, and blacks. *Pediatrics* 2003;111(1):e61-6.
2. Barker DJ. Fetal origins of coronary heart disease. *Bmj* 1995;311(6998):171-4.
3. Bergvall N, Iliadou A, Tuvemo T, Cnattingius S. Birth characteristics and risk of low intellectual performance in early adulthood: are the associations confounded by socioeconomic factors in adolescence or familial effects? *Pediatrics* 2006;117(3):714-21.
4. Caudri D, Wijga A, Gehring U, Smit HA, Brunekreef B, Kerkhof M, et al. Respiratory symptoms in the first 7 years of life and birth weight at term: the PIAMA Birth Cohort. *Am J Respir Crit Care Med* 2007;175(10):1078-85.
5. Leon DA, Lithell HO, Vagero D, Koupilova I, Mohsen R, Berglund L, et al. Reduced fetal growth rate and increased risk of death from ischaemic heart disease: cohort study of 15 000 Swedish men and women born 1915-29. *Bmj* 1998;317(7153):241-5.
6. Hediger ML, Overpeck MD, Maurer KR, Kuczmarski RJ, McGlynn A, Davis WW. Growth of infants and young children born small or large for gestational age: findings from the Third National Health and Nutrition Examination Survey. *Arch Pediatr Adolesc Med* 1998;152(12):1225-31.
7. Lunde A, Melve KK, Gjessing HK, Skjaerven R, Irgens LM. Genetic and environmental influences on birth weight, birth length, head circumference, and gestational age by use of population-based parent-offspring data. *Am J Epidemiol* 2007;165(7):734-41.
8. Jansen PW, Tiemeier H, Looman CWN, Jaddoe VWV, Hofman A, Moll HA, et al. Explaining educational inequalities in birthweight. The Generation R Study. *Paediatr Perinat Epidemiol*.
9. Mortensen LH, Diderichsen F, Arntzen A, Gissler M, Cnattingius S, Schnor O, et al. Social inequality in fetal growth: a comparative study of Denmark, Finland, Norway and Sweden in the period 1981-2000. *J Epidemiol Community Health* 2008;62(4):325-31.
10. Hansen CA, Barnett AG, Pritchard G. The effect of ambient air pollution during early pregnancy on fetal ultrasonic measurements during mid-pregnancy. *Environ Health Perspect* 2008;116(3):362-9.
11. Di Battista E, Bertino E, Benso L, Fabris C, Aicardi G, Pagliano M, et al. Longitudinal distance standards of fetal growth. Intrauterine and Infant Longitudinal Growth Study: IILGS. *Acta Obstet Gynecol Scand* 2000;79(3):165-73.
12. Kramer MS, Olivier M, McLean FH, Dougherty GE, Willis DM, Usher RH. Determinants of fetal growth and body proportionality. *Pediatrics* 1990;86(1):18-26.
13. Jaddoe VW, Mackenbach JP, Moll HA, Steegers EA, Tiemeier H, Verhulst FC, et al. The Generation R Study: Design and cohort profile. *Eur J Epidemiol* 2006;21(6):475-84.
14. Savitz DA, Kaufman JS, Dole N, Siega-Riz AM, Thorp JM, Jr., Kaczor DT. Poverty, education, race, and pregnancy outcome. *Ethn Dis* 2004;14(3):322-9.
15. Allochtonen in Nederland 2004. Voorburg/Heerlen: Statistics Netherlands, 2004.
16. Standaard Onderwijsindeling 2003. Voorburg/Heerlen: Statistics Netherlands, 2004.
17. Verburg BO, Steegers EA, De Ridder M, Snijders RJ, Smith E, Hofman A, et al. New charts for ultrasound dating of pregnancy and assessment of fetal growth: longitudinal data from a population-based cohort study. *Ultrasound Obstet Gynecol* 2008;31(4):388-96.
18. Gynaecologists. RCoOa. Routine ultrasound screening in pregnancy: protocol. In: Press R, editor. London, United Kingdom, 2000.
19. Hadlock FP, Harrist RB, Carpenter RJ, Deter RL, Park SK. Sonographic estimation of fetal weight. The value of femur length in addition to head and abdomen measurements. *Radiology* 1984;150(2):535-40.

20. McNamee R. Confounding and confounders. *Occup Environ Med* 2003;60(3):227-34; quiz 164, 234.
21. Goldstein H. *Multilevel statistical models*. 2nd ed. London: Edward Arnold, 1995.
22. Royston P, Ambler G, Sauerbrei W. The use of fractional polynomials to model continuous risk variables in epidemiology. *Int J Epidemiol* 1999;28(5):964-74.
23. Rubin DB. *Multiple Imputation for Nonresponse in Surveys*. New York: NY: John Wiley & Sons, 1987.
24. Galobardes B, Shaw M, Lawlor DA, Lynch JW, Davey Smith G. Indicators of socioeconomic position (part 1). *J Epidemiol Community Health* 2006;60(1):7-12.
25. Braveman PA, Cubbin C, Egerter S, Chideya S, Marchi KS, Metzler M, et al. Socioeconomic status in health research: one size does not fit all. *Jama* 2005;294(22):2879-88.
26. Parker JD, Schoendorf KC, Kiely JL. Associations between measures of socioeconomic status and low birth weight, small for gestational age, and premature delivery in the United States. *Ann Epidemiol* 1994;4(4):271-8.
27. Center for Research and Statistics, Rotterdam (COS), 2005: http://www.cos.rotterdam.nl.
28. Tunon K, Eik-Nes SH, Grottum P. A comparison between ultrasound and a reliable last menstrual period as predictors of the day of delivery in 15,000 examinations. *Ultrasound Obstet Gynecol* 1996;8(3):178-85.
29. Milani S, Bossi A, Bertino E, di Battista E, Coscia A, Aicardi G, et al. Differences in size at birth are determined by differences in growth velocity during early prenatal life. *Pediatr Res* 2005;57(2):205-10.
30. Roza SJ, Verburg BO, Jaddoe VW, Hofman A, Mackenbach JP, Steegers EA, et al. Effects of maternal smoking in pregnancy on prenatal brain development. The Generation R Study. *Eur J Neurosci* 2007;25(3):611-7.
31. Godfrey K, Robinson S, Barker DJ, Osmond C, Cox V. Maternal nutrition in early and late pregnancy in relation to placental and fetal growth. *Bmj* 1996;312(7028):410-4.
32. Silva A, Metha Z, O'Callaghan F J. The relative effect of size at birth, postnatal growth and social factors on cognitive function in late childhood. *Ann Epidemiol* 2006;16(6):469-76.
33. Leary S, Fall C, Osmond C, Lovel H, Campbell D, Eriksson J, et al. Geographical variation in relationships between parental body size and offspring phenotype at birth. *Acta Obstet Gynecol Scand* 2006;85(9):1066-79.
34. de Vries H, Bakker M, Mullen PD, van Breukelen G. The effects of smoking cessation counseling by midwives on Dutch pregnant women and their partners. *Patient Educ Couns* 2006;63(1-2):177-87.

APPENDIX 1.

MODEL STRUCTURES FOR ANALYSES WITH ESTIMATED FETAL WEIGHT, HEAD CIRCUMFERENCE, ABDOMINAL CIRCUMFERENCE AND FEMUR LENGTH

Estimated fetal weight $= ß_0 + ß_1$*educational level $+ ß_2$*gestational age + $ß_3$ * ln(gestational age) + $ß_4$*gestational age*ln(gestational age) + $ß_5$*educational level gestational age + $ß_6$* educational level *ln(gestational age).

Head circumference $= ß_0 + ß_1$*educational level $+ ß_2$*gestational age $+ ß_3$*gestational age^2 + $ß_4$*gestational age^2*ln(gestational age) + $ß_5$*educational level *gestational age.

Abdominal circumference $= ß_0 + ß_1$*educational level $+ ß_2$*gestational age $+ ß_3$*gestational age^2 + $ß_4$*gestational age^2*ln(gestational age) + $ß_5$*educational level *gestational age.

Femur length $= ß_0 + ß_1$*educational level $+ ß_2$*gestational age $+ ß_3$*gestational age^3 + $ß_4$*educational level*gestational age.

BEST-FITTING MODEL FOR ANALYSES WITH STANDARD-DEVIATION (SD) SCORES FOR ESTIMATED FETAL WEIGHT, HEAD CIRCUMFERENCE, ABDOMINAL CIRCUMFERENCE AND FEMUR LENGTH

SD score $= ß_0 + ß_1$*educational level $+ ß_2$*gestational age $+ ß_3$*educational level*gestational age.

APPENDIX 2. ESTIMATED FETAL WEIGHT, HEAD CIRCUMFERENCE, ABDOMINAL CIRCUMFERENCE AND FEMUR LENGTH AT MEDIAN GESTATIONAL AGE IN MID AND LATE PREGNANCY IN THE TOTAL STUDY POPULATION.

	MID PREGNANCY (MEDIAN 20.5 WEEKS)	LATE PREGNANCY (MEDIAN: 30.4 WEEKS)
Estimated fetal weight (grams)	371.9 (43.7)	1622.0 (188.7)
Head circumference (mm)	178.1 (6.3)	285.4 (9.3)
Abdominal circumference (mm)	155.9 (8.2)	264.6 (13.2)
Femur length (mm)	33.1 (1.8)	57.4 (2.2)

Values are means (with standard deviations)

CHAPTER **2.2**

Explaining educational inequalities in preterm birth

ABSTRACT

BACKGROUND: Although a low socioeconomic status has consistently been associated with an increased risk of preterm birth, little is known about the pathways through which socioeconomic disadvantage influences preterm birth.
AIM: To examine mechanisms that might underlie the association between the educational level of pregnant women as an indicator of socio-economic status, and preterm birth.
METHODS: The study was nested in a population-based cohort study in the Netherlands. Information was available for 3830 pregnant women of Dutch origin.
FINDINGS: The lowest educated pregnant women had a statistically significant higher risk of preterm birth (OR=1.89 [95% CI: 1.28, 2.80]) than the highest educated women. This increased OR was reduced by up to 22% after separate adjustment for age, height, pre-eclampsia, intrauterine growth restriction, financial concerns, long lasting difficulties, psychopathology, smoking habits, alcohol consumption, and BMI of the pregnant women. Joint adjustment for these variables resulted in a reduction of 89% of the increased risk of preterm birth among low educated pregnant women (fully adjusted OR=1.10 [95% CI: 0.66, 1.84]).
CONCLUSIONS: Pregnant women with a low educational level have a nearly two-fold higher risk of preterm birth than women with a high educational level. This elevated risk could largely be explained by pregnancy characteristics, indicators of psychosocial well-being, and lifestyle habits. Apparently, educational inequalities in preterm birth go together with an accumulation of multiple adverse circumstances among women with a low education. A number of explanatory mechanisms unravelled in the present study seem to be modifiable by intervention programs.

WHAT IS ALREADY KNOWN ON THIS TOPIC

- Low socioeconomic status has often been associated with an elevated risk of preterm birth.
- A pregnant woman's age and smoking habits explain part of the association between socioeconomic status and preterm birth, but these factors cannot explain the whole association.

WHAT THIS STUDY ADDS

- Pregnant women with a low SES, as indicated by their educational level, had a nearly two-fold higher risk of preterm birth than pregnant women with a high SES.
- Educational inequalities in preterm birth resulted from an unfavourable combination of various pregnancy characteristics, psychosocial factors, and lifestyle habits, that was present in lower educated women.

INTRODUCTION

Preterm birth is strongly related to perinatal mortality.[1,2] Furthermore, infants born preterm are vulnerable to complications and morbidity in the neonatal phase as well as in later life.[1,3] Research on socioeconomic inequalities in birth outcome across different industrialized countries has indicated that low educational level, low occupational status, and high deprivation scores are associated with an increased risk of preterm birth.[4-10] Only few studies found no relation between socioeconomic status (SES) and preterm birth.[11,12] Despite the abundance of studies describing SES inequalities in preterm birth, little research has evaluated the pathways through which socioeconomic disadvantage influences preterm birth: either no possible explanatory variables were taken into account[8-10] or only a few, such as age, height, and smoking habits of pregnant women.[4-6] However, these few variables could not fully explain the SES variation in preterm birth.[4-6] In two recent reviews it is hypothesized that psychosocial risk factors and unhealthy lifestyle habits may explain part of the SES inequalities in preterm birth, since these variables are both determinants of preterm birth and more prevalent among women in the lower SES strata.[13,14] This hypothesis has not yet been verified.

In the present study we applied educational level of pregnant women as an indicator of SES. Our objective was to examine the association between education and preterm birth. Additionally, we explored whether the educational inequalities in preterm birth could be explained by pregnancy characteristics, psychosocial factors, and lifestyle habits. For this, we used data from the Generation R Study, a large prospective birth-cohort study. The present study involved ethnic Dutch participants only, as educational inequalities in pregnancy outcome and the related explanatory mechanisms may differ between Dutch women and women with another ethnic background.[13,15]

METHODS

DESIGN

This study was nested in the Generation R Study, a population-based cohort study from fetal life until young adulthood.[16,17] All pregnant women living in the study area in Rotterdam, the Netherlands, were informed about the study by health care workers (e.g. community midwives and obstetricians). In total, 8880 pregnant women of different ethnicities with a delivery date between April 2002 and January 2006 enrolled in the prenatal part of the study (response rate 61%). 69% of all participants enrolled in early pregnancy (<18 weeks' gestation). Written informed consent was obtained from all participants. The Medical Ethical Committee of the Erasmus Medical Center, Rotterdam, has approved the study.

POPULATION FOR ANALYSIS

Of the 8880 women who enrolled in the Generation R Study during pregnancy, those with a Dutch ethnicity were selected for the present study (n=4057). Participants with missing data on education (n=21) or gestational age (n=46) were excluded. We also excluded twin pregnancies (n=54), as preterm birth rates differ considerably between singleton and multiple births.[2 18] Women who enrolled after 25 weeks' gestation were excluded (n=106), since pregnancy dating based on ultrasound becomes less reliable as pregnancy proceeds,[19] yielding a sample size of 3830 participants. In 8.5% of the 3830 women, the pregnancy was their second or third pregnancy in the study. Since there were no differences in results after exclusion of these pregnancies, they were included in the analyses.

EDUCATIONAL LEVEL

The highest attained educational level of the participants was assessed by questionnaire. Following the definition of Statistics Netherlands,[20] education was categorized as low (primary school; lower vocational training; intermediate general school; 3 years general secondary school); mid-low (>3 years general secondary school; intermediate vocational training; 1st year higher vocational training); mid-high (higher vocational training; Bachelor's degree); and high (higher academic education; PhD).

PRETERM BIRTH

Gestational age was determined by fetal ultrasound examination at the first visit to our research centre. Pregnancy dating curves were constructed using subjects of whom we had both ultrasound examinations <25 weeks' gestation and reliable information on last menstrual period.[21] Subsequently, all pregnancies in our study were dated using these curves; the crown-rump length was used for pregnancy dating up to 65 mm (n=1351) and biparietal diameter was used for pregnancy dating from 23 mm onwards (n=2479). This corresponds to 12^{+5} weeks' gestation. Information on date of birth was obtained from midwife and hospital registries. Birth was classified as preterm if it occurred <37 weeks' gestation.

COVARIATES

The choice of covariates that might explain the association between educational level and preterm birth, was based on the literature on determinants of preterm birth.[1 7 13 14]

Information on gender, pre-eclampsia, and intrauterine growth restriction (IUGR) was obtained from midwife and hospital registries. Age, height and weight of the pregnant women were assessed at enrolment. Body mass index (BMI) was calculated (kg/m^2). The following covariates were assessed by questionnaire: parity, which we defined as the number of live births the participants previously delivered (0, ≥1); marital status (married/cohabiting, single motherhood); whether the pregnancy was planned (yes, no); financial concerns (no, some, great); smoking habits during pregnancy (non-smoking, smoked until pregnancy was known, continued smoking); and alcohol consumption in mid- and late pregnancy (non-drinking, <1 drink

per week, 1-6 drinks per week, ≥1 drink per day). Long Lasting Difficulties during the year preceding the pregnancy were evaluated with an 12 item-checklist.[22] We assessed psychopathology using the Brief Symptom Inventory, which consists of 53 positive and negative self-appraisal statements.[23] In late pregnancy we asked the participants to report on weekly working hours.

STATISTICAL ANALYSES

The association between educational level of the pregnant women and preterm birth was examined using logistic regression analysis (reference group: highest education). This association adjusted for parity and gender was presented as the basic model (BM). We assessed whether the covariates explained (part of) the differences in risk of preterm birth between the educational groups by separately adding the covariates to the BM. We calculated the percentage change in odds ratios (ORs) per educational category brought about by adding a covariate to the BM ($100 * [OR_{BM} - OR_{extended\ model}] / [1 - OR_{BM}]$). Finally, the BM was adjusted for all covariates that led to a change of more than 5% in ORs in the above analyses. We conducted the final analysis with and without the covariates preeclampsia and IUGR, as these covariates are very proximal factors and thereby, the risk of overcontrolling emerges.

To substitute missing data on the covariates, multiple imputation (function AregImpute in S-Plus 6.0) was applied, using the relations between the variables in the dataset. Since the procedure was repeated five times, multiple imputation took account of the uncertainty of the imputed values.[24] The percentages of missing values per covariate were all below 17%. Complete data was available in 69% of the subjects, 30% of the subjects had less than four missing values on covariates, and 1% had four or more covariates imputed.

The statistical analyses were repeated within the subgroup of women who went in labour spontaneously. We also repeated the analyses within the subgroup of women who provided complete information (complete-case analysis). All statistical analyses were performed using the Statistical Package of Social Sciences version 11.0 for Windows (SPSS Inc, Chicago, IL, USA) and S-Plus 6.0 Professional Release 1 (Insightful Corp., Seattle, WA, USA).

RESULTS

GENERAL CHARACTERISTICS

TABLE 1 shows the general characteristics of the study population per educational level. The mean age of all pregnant women in the study population was 31.3 years (SD=4.5). The lowest educated women were younger (F-test=192; df=3; $p<0.001$) and had higher psychopathology scores (F-test=54; df=3; $p<0.001$) than women with the highest education. Compared to the highest educated pregnant women, the lowest educated women had an increased risk of preterm birth (OR=1.89 [95% CI: 1.28, 2.80]).

TABLE 1. GENERAL CHARACTERISTICS IN THE TOTAL STUDY POPULATION AND BY EDUCATIONAL LEVEL OF THE PREGNANT WOMEN

		LEVEL OF EDUCATION				
	TOTAL (N=3830)	HIGH (N=1264)	MID-HIGH (N=955)	MID-LOW (N=973)	LOW (N=638)	OVERALL P-VALUE*
PREGNANCY CHARACTERISTICS						
Pregnant women's age (years)	31.3 (4.5)	33.0 (3.1)	32.0 (3.7)	30.1 (4.7)	28.6 (5.5)	<0.001
Pregnant women's height (cm)	170.8 (6.4)	171.5 (6.1)	171.4 (6.3)	170.6 (6.4)	168.9 (6.7)	<0.001
Pre-eclampsia (% yes)	1.9	1.2	1.1	2.5	3.6	<0.001
IUGR (% yes)	1.4	0.9	1.2	1.7	2.3	0.076
Parity (% primipara)	59.8	56.9	61.5	63.8	55.7	<0.001
Infant gender (% girls)	49.9	49.6	49.4	51.6	48.5	0.631
PSYCHOSOCIAL FACTORS						
Marital status (% single)	7.6	3.3	4.2	8.2	20.1	<0.001
Pregnancy planning (% not planned)	18.5	10.1	16.0	21.6	34.0	<0.001
Financial concerns						
No concerns (%)	88.4	95.5	91.1	85.8	69.7	<0.001
Some concerns (%)	10.4	4.3	8.2	13.2	25.2	
Great concerns (%)	1.2	0.3	0.7	1.1	5.0	
Long Lasting Difficulties (score)	1.08 (1.0–2.9)	1.08 (1.0–2.6)	1.08 (1.0–2.3)	1.09 (1.0–2.6)	1.17 (1.0–2.9)	<0.001
Psychopathology (score)	0.12 (0.0– 3.0)	0.10 (0.0–2.2)	0.12 (0.0–1.7)	0.13 (0.0–3.0)	0.17 (0.0–2.6)	<0.001
Working hours (hours)	27.4 (13.6)	32.5 (10.8)	27.9 (11.9)	25.1 (14.0)	17.6 (15.8)	<0.001

TABLE 1. CONTINUED

	TOTAL (N=3830)	LEVEL OF EDUCATION HIGH (N=1264)	MID-HIGH (N=955)	MID-LOW (N=973)	LOW (N=638)	OVERALL P-VALUE*
LIFESTYLE HABITS						
Smoking						
No (%)	73.4	87.1	78.6	69.4	46.1	<0.001
Until pregnancy known (%)	9.0	7.8	9.7	10.1	8.8	
Continued during pregnancy (%)	17.5	5.1	11.7	20.6	45.1	
Alcohol consumption¶						
No (%)	50.2	32.4	45.2	64.0	74.9	<0.001
<1 drink per week (%)	34.0	43.4	37.2	26.9	19.9	
1-6 drinks per week (%)	14.8	23.5	15.6	8.6	4.7	
≥1 drink per day (%)	1.0	0.7	1.9	0.5	0.5	
BMI (kg/m²)						
< 18 (%)	0.7	0.6	0.4	0.7	1.1	<0.001
18 – 25 (%)	66.7	75.4	72.7	60.0	50.8	
> 25 (%)	32.6	24.0	26.9	39.3	48.1	
OUTCOME						
Gestational duration						
≥ 37 weeks	95.2	95.6	95.9	96.2	92.0	0.002
34 - 36 weeks	3.6	3.4	3.4	2.7	5.5	
< 34 weeks	1.2	1.0	0.7	1.1	2.5	
OR preterm birth (< 37 weeks) # (95% CI)		Reference	0.89 (0.59, 1.36)	0.82 (0.54, 1.26)	1.89 (1.28, 2.80)	

Values are means (SD) for continuous normally distributed variables, medians (100% range) for continuous non-normally distributed variables, and percentages for categorical variables, for the total population and by level of education.

** ANOVA for continuous normally distributed variables, Kruskal-Wallis test for continuous non-normally distributed variables, and χ^2 test for categorical variables.*

 # Adjusted for parity of the pregnant woman and gender of the child.

¶ Due to the small number of women (n=35) in the category '≥1 drink per day' this category was merged with the category '1-6 drinks per week' in all other analyses.

COVARIATES

TABLE 2 illustrates the explanatory effect of several covariates on the association between educational level of the pregnant women and preterm birth. Separate addition of marital status, pregnancy planning, and working hours to the basic model resulted in changes in ORs for preterm birth of less than 5%. Therefore, these covariates were not included in further analyses. Separate addition of participants' age, height, pre-eclampsia, IUGR, financial concerns, Long Lasting Difficulties, psychopathology, smoking habits, alcohol consumption, and BMI to the basic model substantially (i.e. 5-22%) decreased the ORs of preterm birth in the various educational subgroups as compared to the highest education. The most marked decreases in OR were observed in the lowest educated women. For instance, Long Lasting Difficulties accounted for 9% of the increased OR for preterm birth in the lowest educational group, while this covariate decreased the ORs by 1% in mid-high and 3% in mid-low educated women.

TABLE 2. OR FOR PRETERM BIRTH BY LEVEL OF EDUCATION (REFERENCE: HIGH EDUCATION) AFTER ADJUSTMENT FOR EACH COVARIATE SEPARATELY AND THE CORRESPONDING CHANGE (%) IN OR RELATIVE TO THE BASIC MODEL

	OR FOR PRETERM BIRTH BY LEVEL OF EDUCATION			
	HIGH (N=1264)	**MID-HIGH (N=955)**	**MID-LOW (N=973)**	**LOW (N=638)**
MODEL 1 (BASIC MODEL, BM) #	Reference	0.89 (0.59, 1.36)	0.82 (0.54, 1.26)	1.89 (1.28, 2.80)
PREGNANCY CHARACTERISTICS				
BM + pregnant women's age	Reference	0.87 (0.57, 1.33)	0.77 (0.50, 1.19)	1.69 (1.10, 2.60)
BM + pregnant women's height	Reference	0.89 (0.58, 1.35)	0.79 (0.52, 1.21)	1.69 (1.13, 2.51)
BM + pre-eclampsia	Reference	0.90 (0.59, 1.37)	0.79 (0.51, 1.20)	1.77 (1.19, 2.63)
BM + IUGR	Reference	0.88 (0.58, 1.34)	0.78 (0.51, 1.20)	1.78 (1.19, 2.65)
PSYCHOSOCIAL FACTORS				
BM + marital status	Reference	0.89 (0.59, 1.36)	0.83 (0.54, 1.26)	1.91 (1.28, 2.86)
BM + pregnancy planning	Reference	0.89 (0.59, 1.36)	0.82 (0.54, 1.26)	1.89 (1.26, 2.84)
BM + financial concerns	Reference	0.88 (0.58, 1.33)	0.79 (0.52, 1.22)	1.72 (1.13, 2.60)
BM + Long Lasting Difficulties	Reference	0.88 (0.58, 1.34)	0.80 (0.52, 1.23)	1.79 (1.19, 2.69)
BM + psychopathology	Reference	0.88 (0.58, 1.33)	0.79 (0.51, 1.21)	1.75 (1.16, 2.62)
BM + working hours	Reference	0.89 (0.58, 1.37)	0.82 (0.53, 1.28)	1.89 (1.21, 2.98)
LIFESTYLE HABITS				
BM + smoking habits	Reference	0.89 (0.58, 1.35)	0.81 (0.53, 1.25)	1.82 (1.19, 2.78)
BM + alcohol consumption	Reference	0.86 (0.57, 1.32)	0.80 (0.51, 1.23)	1.74 (1.15, 2.64)
BM + BMI	Reference	0.89 (0.59, 1.35)	0.81 (0.53, 1.24)	1.83 (1.23, 2.73)

Values are odds ratios (95% CI): risk for preterm birth compared to the reference group (high education), and corresponding change (%) in OR relative to the basic model and due to the covariate.
 # BM: adjusted for parity of the pregnant woman and gender of the child.

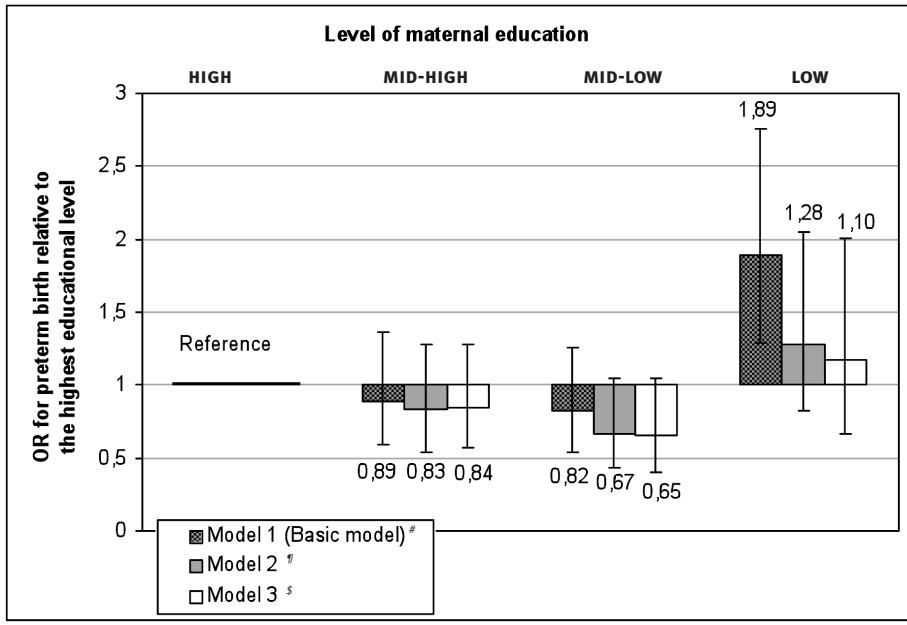
TABLE 3 and FIGURE 1 show the association of educational level with preterm birth after adjustment for all covariates that independently led to a significant change in the separate analyses. Full adjustment for the covariates resulted in a reduction of 89% of the increased risk of preterm birth among low educated women (parity and gender adjusted OR: 1.89 [95% CI: 1.28, 2.80]; fully adjusted OR: 1.10 [95% CI:0.66, 1.84]). In none of the educational groups the fully adjusted ORs were statistically significant. The difference between the models with and without the covariates pre-eclampsia and IUGR was marginal for the mid-high and mid-low educated women, while among the low educated women these covariates led to a further reduction of the OR on top of the other covariates (reduction model 2: 69%; reduction model 3: 89%).

TABLE 3. RISK OF PRETERM BIRTH IN THE EDUCATIONAL GROUPS AFTER ADJUSTMENT FOR ALL RELEVANT COVARIATES

		REGRESSION COEFFICIENTS (95% CI)		
VARIABLES	**CATEGORIES**	**MODEL 1 (BM #)**	**MODEL 2**	**MODEL 3**
Maternal education	High	Reference	Reference	Reference
	Mid-high	0.81 (0.53, 1.25)	0.83 (0.54, 1.27)	0.81 (0.53, 1.25)
	Mid-low	0.65 (0.41, 1.04)	0.67 (0.42, 1.07)	0.65 (0.41, 1.04)
	Low	1.10 (0.66, 1.84)	1.28 (0.78, 2.12)	1.10 (0.66, 1.84)
Parity	Primipara	1.41 (0.99, 2.00)	1.61 (1.15, 2.27)	1.41 (0.99, 2.00)
Gender	Girl	0.83 (0.61, 1.13)	0.89 (0.66, 1.21)	0.83 (0.61, 1.13)
Maternal age			0.93 (0.76, 1.13)	0.88 (0.72, 1.08)
Maternal height			0.71 (0.59, 0.86)	0.74 (0.61, 0.90)
Pre-eclampsia	Yes			4.73 (2.49, 9.00)
IUGR	Yes			8.31 (4.32, 15.99)
Financial concerns	No concerns		Reference	Reference
	Some concerns		1.38 (0.86, 2.23)	1.36 (0.79, 2.33)
	Great concerns		1.43 (0.44, 4.67)	1.13 (0.31, 4.16)
Long Lasting Difficulties			0.98 (0.80, 1.20)	0.95 (0.75, 1.20)
Psychopathology			1.04 (0.91, 1.19)	1.10 (0.96, 1.26)
Smoking habits	No		Reference	Reference
	Until pregnancy known		1.03 (0.60, 1.76)	1.05 (0.60, 1.81)
	Continued during pregnancy		0.97 (0.62, 1.50)	1.01 (0.65, 1.58)
Alcohol consumption	No		Reference	Reference
	<1 drink per week		0.85 (0.60, 1.22)	0.86 (0.60, 1.24)
	≥1 drink per week		0.78 (0.47, 1.30)	0.80 (0.48, 1.34)
BMI	< 18		1.43 (0.32, 6.31)	1.60 (0.36, 7.05)
	18 – 25		Reference	Reference
	> 25		1.06 (0.77, 1.47)	1.05 (0.75, 1.46)

 # BM is basic model.

FIGURE 1. UNADJUSTED AND FULLY ADJUSTED OR FOR PRETERM BIRTH (REFERENCE: HIGH EDUCATION)



 # Model 1 (Basic model): Adjusted for parity of pregnant women and gender of the children.
¶ Model 2: Model 1 additionally adjusted for pregnant women's age, pregnant women's height, financial concerns, Long Lasting Difficulties, psychopathology, smoking habits, alcohol consumption, and BMI.
$ Model 3: Model 2 additionally adjusted for pre-eclampsia and IUGR.

The association between educational level and preterm birth in the subgroup of women who went in labour spontaneously (n=2474) was comparable to the results of the whole study population (n=3830). The complete-case sample (n=2642) consisted of 74% of the high educated, 75% of the mid-high educated, 66% of the mid-low educated, and of 55% of the low educated women of the initial study population. Preterm birth was less prevalent in the complete-case sample (4.1%) than in the total study population (4.8%). Moreover, the risk of preterm birth in the lowest educated women (OR=1.68 [95% CI: 0.98, 2.86]) was smaller in the complete-case sample than in the total study population. In the fully adjusted model, the OR attenuated to 0.80 [95% CI: 0.40, 1.61].

DISCUSSION

This prospective population-based study showed that women with a low educational level had a nearly two-fold higher risk of preterm birth compared to women with a high educational level. This elevated risk was roughly explained by an unfavourable combination of pregnancy characteristics, psychosocial well-being, and lifestyle habits, that was present in lower educated women.

In our study, only the subgroup of women with the lowest educational level had a significantly increased risk for preterm birth as compared to the subgroup of high educated women. Previous studies using other indicators of SES reported an inverse linear trend between SES level and risk of preterm birth.[4-10] Future studies, preferably with larger samples, should verify whether only very low educated women are at risk for preterm birth or whether our findings occurred by chance. The magnitude of the odds ratio for preterm birth among low versus high educated women compares well with earlier findings from Western countries.[4-10] For instance, Peacock *et al.* also reported the prevalence of preterm birth in the U.K. roughly to be twice as high in the lower SES strata as compared to high SES.[9]

EXPLANATION OF RISK OF PRETERM BIRTH

The current study explained a substantial amount, i.e. 89%, of the elevated risk of preterm birth among the lowest educated women. This was accomplished by including a comprehensive set of potential explanatory factors, namely adverse pregnancy characteristics, psychosocial variables and lifestyle factors, that were chosen on the basis of existing knowledge.[1 7 13 14] Besides a on average younger age and shorter height, women with a low SES seem to have an accumulation of adverse circumstances, especially regarding psychosocial stress and unhealthy lifestyle habits, that turned out to be associated with their increased risk of preterm birth. Previous studies on SES inequalities in preterm birth explained at best 65% of the increased risk among lower SES women. However, in these studies only a limited number of explanatory factors was included.[4-7]

Pregnancy characteristics

In our study, a relatively high prevalence of pre-eclampsia and IUGR was found among lower educated women. Since both pre-eclampsia and IUGR are highly associated with and often the direct cause of preterm birth, these medical conditions explained part of the increased risk of preterm birth among low educated women. Preterm birth due to pre-eclampsia or IUGR can occur spontaneously or may be induced to reduce health risks in both mother and child.[25 26] The fully adjusted analyses with and without pre-eclampsia and IUGR indicated that, only among the lowest educated women, these two conditions explained an additional part of the elevated risk of preterm birth.

Indicators of psychosocial stress

Psychosocial factors, such as financial concerns, 'Long Lasting Difficulties', and psychopathology of the pregnant women explained a substantial part of the increased risk of preterm birth among low educated women. This finding is in line with theories on the effects of prenatal stress, in which psychosocial stress is hypothesized to be associated with a relatively higher risk of preterm birth through specific patterns of a pregnant woman's physiological and hormonal response to stress.[27 28]

Lifestyle habits

With regard to BMI, a factor that we consider as an indicator of physical activity and diet, both overweight (BMI>25) and especially thinness (BMI<18) are well established risk factors for preterm birth.[13 29 30] In our study, BMI clearly contributed to the explanation of educational differences in risk of preterm birth. We hypothesize that the impact of overweight on preterm birth among low educated women is larger than the impact of thinness, since overweight is much more prevalent in this educational subgroup than thinness.

We showed that continuation of alcohol consumption during pregnancy, which is relatively less common among women with low education as compared to higher educated women, also explained a considerable part of the educational inequalities in preterm birth. It is hypothesized that low to moderate alcohol consumption during pregnancy may be genuinely beneficial, although the effects may also be explained by the 'healthy drinker effect', in which women with a poor obstetric history are more likely to abstain from drinking.[31] Clearly, further research is required to test these hypotheses.

STRENGTHS AND LIMITATIONS

The strengths of the present study are the large number of participating pregnant women with different levels of education, its prospective population-based design and the detailed information on numerous relevant covariates. Another strong point is that gestational duration was established by fetal ultrasound examination, as using the last menstrual period has several limitations, including the large number of women who do not know the exact date of their last menstrual period or have irregular menstrual cycles.[32] A final strength of the study is the thorough missing values procedure that was applied. We decided to impute missing data instead of excluding those with missing values, as multiple imputation has the benefit of circumventing selection mechanisms involved in missing values, namely that data was more complete in higher educated women and among those having a term delivery. Moreover, using multiple imputation instead of complete case analysis also increased statistical power due to a larger study population.

Some methodological issues need to be considered. The participants of the Generation R cohort represent a selection towards a somewhat more healthy population.[17 33] Additionally, our study was limited by the availability of covariates; e.g. we did not assess the influence of pregnancy interval, dietary intake, bacterial vaginosis, and other stressful circumstances than the ones included. These factors

potentially contribute to the explanation of educational inequalities in preterm birth. Finally, it is possible that different educational groups are characterized by different lifestyles and behaviours in various societies, which for instance may be the case regarding alcohol consumption during pregnancy. Therefore, some caution is needed when generalizing our results to other populations.

CONCLUSIONS

Given the nearly two-fold higher risk of preterm birth among low educated women and the associated medical consequences in the neonatal phase as well as in later life, it is important to invest in policies aimed at reducing educational inequalities in preterm birth.

Even though risk factors for preterm birth among low educated women may not be easily amendable, there might be opportunities that are not yet applied effectively. Several of the explanatory factors identified in this study, such as young age, stressful circumstances, smoking habits and overweight, are modifiable by up-to-date interventions.[34-37] Initiation of preventive interventions during pregnancy may be too late. Therefore, the most effective strategy for tackling educational inequalities in preterm birth is probably by nesting these programs in preconception care.[38]

REFERENCES

1. Behrman RE, Stith Butler A. *Preterm birth. Causes, consequences, and prevention.* Washington D.C., USA: The National Academies Press, 2007.
2. Demissie K, Rhoads GG, Ananth CV, Alexander GR, Kramer MS, Kogan MD, et al. Trends in preterm birth and neonatal mortality among blacks and whites in the United States from 1989 to 1997. *Am J Epidemiol* 2001;154(4):307-15.
3. Raju TN. The problem of late-preterm (near-term) births: a workshop summary. *Pediatr Res* 2006;60(6):775-6.
4. Ancel PY, Saurel-Cubizolles MJ, Di Renzo GC, Papiernik E, Breart G. Social differences of very preterm birth in Europe: interaction with obstetric history. Europop Group. *Am J Epidemiol* 1999;149(10):908-15.
5. Gissler M, Merilainen J, Vuori E, Hemminki E. Register based monitoring shows decreasing socioeconomic differences in Finnish perinatal health. *J Epidemiol Community Health.* 2003;57(6):433-9.
6. Luo ZC, Wilkins R, Kramer MS. , Fetal and Infant Health Study Group of the Canadian Perinatal Surveillance System. Effect of neighbourhood income and maternal education on birth outcomes: a population-based study. *CMAJ* 2006;174(10):1415-20.
7. Meis PJ, Michielutte R, Peters TJ, Wells HB, Sands RE, Coles EC, et al. Factors associated with preterm birth in Cardiff, Wales. I. Univariable and multivariable analysis. *Am J Obstet Gynecol.* 1995;173(2):590-6.
8. Aszkenasy M, Hutchison S. Births, gestation and birthweights in South Tees 1990-1996. *J Public Health Med* 2000;22(4):457-61.
9. Peacock JL, Bland JM, Anderson HR. Preterm delivery: effects of socioeconomic factors, psychological stress, smoking, alcohol, and caffeine. *BMJ.* 1995;311(7004):531-5.
10. Smith LK, Draper ES, Manktelow BN, Dorling JS, Field DJ. Socioeconomic inequalities in very preterm birth rates. *Arch Dis Child Fetal Neonatal Ed* 2007;92(1):F11-4.
11. Craig ED, Thompson JM, Mitchell EA. Socioeconomic status and preterm birth: New Zealand trends, 1980 to 1999. *Arch Dis Child Fetal Neonatal Ed* 2002;86(3):F142-6.
12. Delpisheh A, Kelly Y, Rizwan S, Brabin BJ. Socio-economic status, smoking during pregnancy and birth outcomes: an analysis of cross-sectional community studies in Liverpool (1993-2001). *J Child Health Care* 2006;10(2):140-8.
13. Kramer MS, Seguin L, Lydon J, Goulet L. Socio-economic disparities in pregnancy outcome: why do the poor fare so poorly? *Paediatr Perinat Epidemiol.* 2000;14(3):194-210.
14. Moutquin JM. Socio-economic and psychosocial factors in the management and prevention of preterm labour. *BJOG.* 2003;110 Suppl 20:56-60.
15. Savitz DA, Kaufman JS, Dole N, Siega-Riz AM, Thorp JM, Jr., Kaczor DT. Poverty, education, race, and pregnancy outcome. *Ethn Dis.* 2004;14(3):322-9.
16. Hofman A, Jaddoe VW, Mackenbach JP, Moll HA, Snijders RF, Steegers EA, et al. Growth, development and health from early fetal life until young adulthood: the Generation R Study. *Paediatr Perinat Epidemiol.* 2004;18(1):61-72.
17. Jaddoe VW, Mackenbach JP, Moll HA, Steegers EA, Tiemeier H, Verhulst FC, et al. The Generation R Study: Design and cohort profile. *Eur J Epidemiol.* 2006;21(6):475-84.
18. Joseph KS, Kramer MS, Marcoux S, Ohlsson A, Wen SW, Allen A, et al. Determinants of preterm birth rates in Canada from 1981 through 1983 and from 1992 through 1994. *N Engl J Med* 1998;339(20):1434-9.
19. Altman DG, Chitty LS. New charts for ultrasound dating of pregnancy. *Ultrasound Obstet Gynecol.* 1997;10(3):174-91.
20. (2004a). Centraal bureau voor de statistiek. Standaard onderwijsindeling 2003. Voorburg/ Heerlen.

21. Verburg BO, Steegers EAP, Ridder MAd, Snijders RJM, Hofman A, Moll HA, et al. New charts for ultrasound dating of pregnancy and assessment of fetal growth: longitudinal data from a population-based cohort study. *Ultrasound Obstet Gynecol.* 2007;In press.
22. Hendriks A, Ormel J, Willige Gvd. Long lasting difficulties measured with a self-assessment questionnaire and semi-structured interview: a theoretical and empirical comparison [in Dutch]. *Gedrag Gezondh.* 1990;18:273-283.
23. Derogatis LR. *Brief Symptom Inventory (BSI): Administration, scoring and procedures. Manual, third edition*. Minneapolis, MN, USA, 1993.
24. Harrell Jr. FE. *Regression Modeling Strategies: With Applications to Linear Models, Logistics Regression, and Survival Analysis*. New York, USA: Springer-Verlag New York, Inc., 2001.
25. Duley L, Meher S, Abalos E. Management of pre-eclampsia. *Bmj* 2006;332(7539):463-8.
26. Hershkovitz R, Erez O, Sheiner E, Bashiri A, Furman B, Shoham-Vardi I, et al. Comparison study between induced and spontaneous term and preterm births of small-for-gestational-age neonates. *Eur J Obstet Gynecol Reprod Biol* 2001;97(2):141-6.
27. Hobel C, Culhane J. Role of psychosocial and nutritional stress on poor pregnancy outcome. *J Nutr.* 2003;133(5 Suppl 2):1709S-1717S.
28. Mulder EJ, Robles de Medina PG, Huizink AC, Van den Bergh BR, Buitelaar JK, Visser GH. Prenatal maternal stress: effects on pregnancy and the (unborn) child. *Early Hum Dev.* 2002;70(1-2):3-14.
29. Ancel PY, Saurel-Cubizolles MJ, Di Renzo GC, Papiernik E, Breart G. Very and moderate preterm births: are the risk factors different? *Br J Obstet Gynaecol* 1999;106(11):1162-70.
30. Honest H, Bachmann LM, Ngai C, Gupta JK, Kleijnen J, Khan KS. The accuracy of maternal anthropometry measurements as predictor for spontaneous preterm birth–a systematic review. *Eur J Obstet Gynecol Reprod Biol* 2005;119(1):11-20.
31. Henderson J, Gray R, Brocklehurst P. Systematic review of effects of low-moderate prenatal alcohol exposure on pregnancy outcome. *Bjog* 2007;114(3):243-52.
32. Morin I, Morin L, Zhang X, Platt RW, Blondel B, Breart G, et al. Determinants and consequences of discrepancies in menstrual and ultrasonographic gestational age estimates. *Bjog* 2005;112(2):145-52.
33. Center for Research and Statistics, Rotterdam (COS). 2005.
34. Bennett SE, Assefi NP. School-based teenage pregnancy prevention programs: a systematic review of randomized controlled trials. *J Adolesc Health* 2005;36(1):72-81.
35. Claesson IM, Sydsjo G, Brynhildsen J, Cedergren M, Jeppsson A, Nystrom F, et al. Weight gain restriction for obese pregnant women: a case-control intervention study. *Bjog* 2008;115(1):44-50.
36. Melvin CL, Dolan-Mullen P, Windsor RA, Whiteside HP, Jr., Goldenberg RL. Recommended cessation counselling for pregnant women who smoke: a review of the evidence. *Tob Control.* 2000;9 Suppl 3:III80-4.
37. Vieten C, Astin J. Effects of a mindfulness-based intervention during pregnancy on prenatal stress and mood: results of a pilot study. *Arch Womens Ment Health* 2008;11(1):67-74.
38. Weerd S, Steegers E. The past and present practices and continuing controversies of preconception care. *Community Genet.* 2002;5(1):50-60.

APPENDIX 1. ASSOCIATIONS OF EXPLANATORY VARIABLES WITH PRETERM BIRTH[#]

	PRETERM BIRTH OR (95% CI)
PREGNANCY CHARACTERISTICS	
Pregnant women's age (per year)	0.81 (0.68, 0.97)
Pregnant women's height (per 10 cm)	0.68 (0.56, 0.82)
Pre-eclampsia (yes vs no)	5.66 (3.15, 10.2)
IUGR (yes vs no)	9.82 (5.42, 17.8)
PSYCHOSOCIAL FACTORS	
Marital status (single vs married/cohabiting)	1.14 (0.67, 1.93)
Pregnancy planning (not planned vs planned)	1.20 (0.82, 1.76)
Financial concerns	
No concerns	Reference
Some concerns	1.58 (1.00, 2.49)
Great concerns	2.09 (0.58, 7.58)
Long Lasting Difficulties (per score point)	1.14 (0.98, 1.31)
Psychopathology (per score point)	1.12 (1.02, 1.23)
Working hours (per hour)	0.90 (0.77, 1.07)
LIFESTYLE HABITS	
Smoking habits	
No	Reference
Until pregnancy known	1.09 (0.59, 2.00)
Continued during pregnancy	1.31 (0.89, 1.92)
Alcohol consumption	
No (%)	Reference
<1 drink per week (%)	0.78 (0.56, 1.10)
≥1 drink per week (%)	0.70 (0.44, 1.13)
BMI (kg/m²)	
‹ 18	1.79 (1.00, 2.49)
18 – 25	Reference
› 25	1.20 (0.88, 1.64)

Values are odds ratios (95% CI).
[#] Adjusted for parity of the pregnant woman and gender of the child.

CHAPTER **2.3**

Explaining educational inequalities in birthweight

ABSTRACT

Although low socioeconomic status has consistently been associated with a lower birthweight, little is known about the factors whereby socioeconomic disadvantage influences birthweight. We therefore examined explanatory mechanisms that might underlie the association between the educational level of pregnant women, as an indicator of socio-economic status, and birthweight. The study was embedded within a population-based cohort study in the Netherlands. Information on maternal education, offspring's birthweights and several determinants of birthweight was available for 3546 pregnant women of Dutch origin. Infants of the lowest educated women had a statistically significantly lower birthweight than infants of the highest educated women (difference adjusted for gender and gestational age: -123 g (95% CI: -167,-79)). Parity, age of the pregnant women, hypertension, parental height and birthweight, marital status, pregnancy planning, financial concerns, number of people in household, weight gain and smoking habits individually explained a statistically significantly part of the differences in birthweight, while adjustment for working hours and body mass index resulted in increases in birthweight differences between the educational levels. After full adjustment, the difference in birthweight between lowest and highest education was reduced by 66%. Our study confirmed remarkable educational inequalities in birthweight, a large part of which was explained by pregnancy characteristics, anthropometrics, psychosocial and material situation, and lifestyle-related factors. Altering smoking habits may be an option to reduce educational differences in birthweight, as many lower educated women tend to continue smoking during pregnancy. In order to tackle inequalities in birthweight, it is crucial that interventions are accessible for pregnant women in lower socioeconomic strata.

INTRODUCTION

Birthweight is strongly related to neonatal mortality.[1 2] The risk of adverse outcomes is seen not only in those with a low birthweight (<2500 g), but in the broad spectrum of birthweight reflected by "the lighter the worse".[3] For infants born at term, Alexander et al[1] reported neonatal mortality rates (per 1000) ranging from below 0.70 in infants weighing over 3250 g, to 3.03 in the 2500-2749 g category —a considerable variation within the normal range of birthweight. Furthermore, studies showed that unfavourable conditions in early fetal life, as expressed in a lower birthweight, are associated with a higher risk of diseases in later life, such as coronary heart disease and stroke.[3 4] Research even indicates that birthweight is related to mental disorder,[5 6] for instance, the risk of schizophrenia being 1.5 times higher per kg decrease in birthweight.[6]

Studies on socioeconomic inequalities in birthweight have consistently associated low educational level, low occupational status, and adverse neighbourhood characteristics with a lower birthweight in offspring.[7-10] These inequalities in birthweight are analogous to the socioeconomic gradient in morbidity and mortality in adult life.[11 12] Given the above described association between birthweight and risk of disease in later life, it seems that socioeconomic inequalities in health throughout life are determined partly by inequalities that originate during fetal life.[10 13] Attempts to tackle the socioeconomic gradient in health should therefore start by reducing inequalities in birthweight.

Some studies have evaluated the mechanisms whereby socioeconomic disadvantage influences birthweight.[7 8 14-18] Most have been register-based, and had only limited data available on the broad set of known determinants of birthweight[19]. In the past, many risk factors for a lower birthweight have been identified, such as shorter gestational duration,[2 20] female gender, being primipara, pregnant women's short height and low body mass index (BMI), smoking habits during pregnancy,[19] and single motherhood[20]. More recently, it was reported that a pregnant woman's exposure to stress, for instance due to an unplanned pregnancy or chronic conditions, also influences birthweight.[21 22] Research concerning psychopathology of pregnant women indicated that high levels of depression and anxiety resulted in reduced birthweight.[21] Differences in prevalence of these risk factors between different SES levels may explain part of the inequalities in birthweight.

In the present study we applied educational level of pregnant women as an indicator of SES.[23 24] Our objective was to identify whether educational inequalities in birthweight could be explained by pregnancy characteristics, anthropometrics, the psychosocial and material situation, and lifestyle-related factors. For this, we used the Generation R Study, a large prospective birth-cohort study of an urban population. As Generation R was specifically designed to observe the impact of constitutional and environmental factors on fetal life and birth outcomes by including participants during the first trimester of pregnancy, it has data available on a wide range of determinants of birthweight. The present study involved ethnic Dutch participants only, as educational inequalities in pregnancy outcome and the

related explanatory mechanisms may differ between Dutch women and women with another ethnic background.[25 26]

METHODS

DESIGN

This study was embedded within the Generation R Study, a prospective population-based cohort study from fetal life until young adulthood. It has been described in detail elsewhere.[27 28] All pregnant women living in the study area in Rotterdam, the Netherlands, were informed about the study by health care workers (e.g. community midwives and obstetricians). In total, 8880 pregnant women of different ethnicities with a delivery date between April 2002 and January 2006 enrolled in the prenatal part of the study. Assessments, including fetal ultrasound examinations and questionnaires, were planned in early pregnancy (<18 weeks' gestation), mid-pregnancy (18-25 weeks' gestation) and late pregnancy (≥25 weeks' gestation). Written informed consent was obtained from all participants. The Medical Ethical Committee of the Erasmus Medical Centre, Rotterdam, has approved the study.

POPULATION FOR ANALYSIS

Of the women who enrolled in the Generation R Study during pregnancy (n=8880), those whose ethnicity was other than Dutch (n=3946) or those with missing data on their ethnicity (n=996) were excluded from the present study. Of the remaining 3938 pregnant women, we excluded twin pregnancies (n=54), since growth potentials for fetuses in multiple pregnancies are not comparable with singleton pregnancies.[29] We excluded those with missing data on educational level (n=105) and birthweight (n=62) as well. Furthermore, preterm births (n=171) were also excluded, since educational differences in birthweight and it's explanatory mechanisms were different for preterm as compared to term births. In total, 3546 subjects were included in the present analysis. Of all eligible infants born to Dutch women in the study area, 68% participated in the study at birth (based on cohort years 2004 and 2005: of the 3425 life births of Dutch women in the study area, 2337 participated).[30]

EDUCATIONAL LEVEL

The highest attained educational level of the participants was assessed by questionnaire. Following the definition of Statistics Netherlands,[31] education was categorized as low (primary school; lower vocational training; intermediate general school; 3 years general secondary school), which typically corresponds to ≤12 years of education; mid-low (>3 years general secondary school; intermediate vocational training; 1st year higher vocational training), in general corresponding with 13-15 years of education; mid-high (higher vocational training; Bachelor's degree), typically matching with 16 or 17 years of education; and high (higher academic education; PhD), usually indicating 18 years of education or more.

BIRTHWEIGHT

Medical records completed by community midwives and obstetricians were used to obtain information about birthweight (in grams) of the infants.

COVARIATES

The covariates specified below were considered as factors that might explain the association between educational level and birthweight; the choice of these covariates was based on the available literature on determinants of birthweight.[19-21 32] All covariates were assessed during pregnancy. Categories are indicated between parentheses.

Pregnancy characteristics

Gestational age was determined by fetal ultrasound examination at the intake visit to our research centre. Pregnancy dating curves were constructed using subjects of whom we had both ultrasound examinations before 25 weeks' gestation and reliable information on last menstrual period.[33] Subsequently, all pregnancies in our study were dated using these curves. Information on date of birth and gender was obtained from midwife and hospital registries. We assessed participants' age on enrolment in the study. Parity was assessed by questionnaire in early pregnancy; we defined parity as the number of live births the participant previously delivered (0, ≥1). Information on hypertension (yes, no) was obtained from the medical records completed by obstetricians. Participants with pre-existing hypertension, pregnancy induced hypertension, or pre-eclampsia were categorized as being hypertensive.

Anthropometrics

Heights of the pregnant women and the fathers of the infants were measured during the initial visit. Information on birthweight of the participants and the fathers of the infants was obtained by questionnaire in early pregnancy (<3000, 3000-4000, >4000 g).

Psychosocial & material situation

Information on marital status of the pregnant women (married/cohabiting, single motherhood) and whether the pregnancy was planned (yes, no) was obtained by questionnaire in early pregnancy. The number of people living in the same household as the participating pregnant woman (including herself) was assessed in mid-pregnancy. In the same questionnaire, psychopathology of the pregnant women was assessed using the Brief Symptom Inventory, a validated self-report questionnaire.[34 35] Participants reported on financial concerns (no, some, great) and working hours (open question) in the questionnaire sent in late pregnancy.

Lifestyle-related factors

Participants' weight (kg) was measured at each visit to the research centre, thus making it possible to determine BMI at intake (BMI: weight/height^2 (kg/m^2)) and weight gain from the first to the third visit (kg). In the analyses both BMI and

weight gain were corrected for gestational age at the time of the visits using the following method. First, we performed a separate linear regression analysis with gestational age at time of visit as predictor and BMI/weight gain as outcome. Next, for every woman the difference between the fitted value at the individual's gestational age at enrolment and the actual observation was added to the expected value at a gestational age of 14 weeks. Smoking habits (non-smoking, smoked <5 per day, smoked ≥5 per day) and alcohol consumption during the second half of pregnancy (no alcohol consumption, <1 per week, ≥1 per week) were assessed by questionnaire in mid- and late pregnancy.

STATISTICAL ANALYSES

Multivariable linear regression analyses were used to examine the association between education and birthweight adjusted for infant gender and gestational age (presented as "basic model" (BM)). The values presented below reflect the differences in birthweight (in grams) between the highest educational group (reference group) and the other educational groups. We assessed whether the covariates could explain part of the birthweight differences by separately adding these variables to the BM. The corresponding percentages of *change* in birthweight differences were calculated by comparing the birthweight differences of the BM with the adjusted ones (100 * (difference in birthweight$_{BM}$ – difference in birthweight$_{\text{model with covariate}}$) / (difference in birthweight$_{BM}$)). A positive percentage of change (accompanying a decrease in differences) denotes how much of the difference in birthweight is explained by the specific covariate. The percentages of change were calculated using a method formulated by Sobel;[36] 95% confidence intervals (95% CI) around the percentages of change and associated p-values were calculated by bootstrap.[37]

To substitute missing data on the covariates, multiple imputation (function AregImpute in Splus 6.0) was applied, using the relations between the variables in the dataset.[38] Because the procedure was repeated five times, multiple imputation took account of the uncertainty of the imputed values. The percentages of missing values per covariate were all below 21%, except for paternal birthweight (44% missing values).

Finally, the BM was adjusted for all covariates that independently led to a significant change (p-value <0.10) in birthweight differences between the educational levels; only psychopathology and alcohol consumption were not included in the fully adjusted model, as these covariates did not lead to a significant change.

The statistical analyses were repeated within the subgroup of women who provided complete information (complete-case analysis). All statistical analyses were performed using the Statistical Package of Social Sciences version 11.0 for Windows (SPSS Inc, Chicago, IL, USA) and Splus 6.0 Professional Release 1.

RESULTS

GENERAL CHARACTERISTICS

TABLE 1 shows the general characteristics of the study population by educational level. On average, the lower educated pregnant women were the youngest (p-value <0.001). Ninety-four percent of the highest educated women were married or cohabiting, 20% of the lowest educated participants were single mothers. Thirty-eight percent of the lowest educated women continued to smoke during pregnancy, compared to 5% in the highest educational group (p-value <0.001). The distribution of missing values per covariate by educational level indicated the tendency that data was more often missing among lower educated women. For instance, data on paternal height was missing among 9.0% of the highest educated women and among 23.2% of the lowest educated women (χ^2=84, p<0.001).

BIRTHWEIGHT CHARACTERISTICS

Mean birthweight ranged from 3424 g (SD 495) in the lowest educational group to 3601 g (SD 484) in the highest, representing an unadjusted mean birthweight difference of 176 g (95% CI: -216, -136) (TABLE 2). The lowest educated mothers had the highest risk of having an infant weighing under 2500 g (p-value <0.001), and the lowest —though statistically non-significant (p-value =0.317)— risk of having a macrosomic baby (>4500 g).

COVARIATES

The effect of separate adjustment for the covariates on the differences in birthweight between the various educational groups is presented in TABLE 3. The basic model, which was adjusted for gender and gestational age, showed mean birthweight differences between the reference and other educational groups of -123 g (low; 95% CI: -167, -79), -60 g (mid-low; 95% CI: -99, -22) and -20 g (mid-high; 95% CI: -58, 19). Adding women's age, paternal height, pregnancy planning, financial concerns and smoking habits to the BM resulted in significantly lower differences in birthweight between highest education and the remaining educational levels (for each covariate: p-value for change <0.10). Parity, hypertension, height and birthweight of the pregnant women, paternal birthweight, marital status, number of people in household and weight gain also led to significantly lower differences in birthweight, but not in all educational groups (see TABLE 3). Addition of BMI and working hours to the BM resulted in significantly higher differences in birthweight between the various educational groups (for each covariate: p-value for change <0.10).

TABLE 1. GENERAL CHARACTERISTICS IN THE TOTAL STUDY POPULATION AND BY LEVEL OF MATERNAL EDUCATION

		LEVEL OF MATERNAL EDUCATION				
	TOTAL (N=3546)[b]	HIGH (N=1162)	MID-HIGH (N=882)	MID-LOW (N=909)	LOW (N=593)	P-VALUE FOR HETEROGENEITY [a]
PREGNANCY CHARACTERISTICS						
Infant gender (% girls)	49.8	49.5	49.5	51.4	48.3	0.684
Gestational age (weeks)	40.2 (1.3)	40.3 (1.2)	40.2 (1.3)	40.1 (1.3)	40.0 (1.3)	<0.001
Maternal age (years)	31.3 (4.5)	33.1 (3.1)	32.0 (3.7)	30.1 (4.7)	28.7 (5.7)	<0.001
Parity						
Primipara (%)	58.0	55.5	59.8	61.7	54.4	0.006
Multipara (%)	40.9	43.6	39.1	37.1	43.8	
Missing (%)	1.2	0.9	1.1	1.2	1.9	
Hypertension						
Yes (%)	7.3	6.2	5.2	9.6	9.1	<0.001
No (%)	91.0	92.3	93.8	88.3	88.4	
Missing (%)	1.7	1.5	1.0	2.1	2.5	
ANTHROPOMETRICS						
Maternal height (cm)	170.9 (6.4)	171.6 (6.1)	171.3 (6.3)	170.7 (6.4)	169.0 (6.7)	<0.001
Maternal birth weight						
<3000 grams (%)	20.8	19.1	18.6	21.6	26.1	<0.001
3000-4000 grams (%)	50.6	53.8	53.7	50.3	40.2	
>4000 grams (%)	8.0	6.9	8.4	9.5	7.2	
Missings (%)	20.6	20.2	19.3	18.7	26.4	
Paternal height (cm)	183.9 (7.2)	185.1 (7.0)	184.0 (7.0)	183.2 (7.4)	182.2 (7.4)	<0.001
Missings (%)	12.6	9.0	9.3	13.4	23.2	
Paternal birth weight						
<3000 grams (%)	9.2	8.3	9.3	9.9	9.4	0.067
3000-4000 grams (%)	36.8	41.1	40.0	35.2	25.9	
>4000 grams (%)	10.0	11.5	10.7	9.5	9.4	
Missings (%)	44.0	39.0	40.0	45.4	57.7	

TABLE 1. CONTINUED

	TOTAL (N=3546)[b]	LEVEL OF MATERNAL EDUCATION				P-VALUE FOR HETEROGENEITY[a]
		HIGH (N=1162)	MID-HIGH (N=882)	MID-LOW (N=909)	LOW (N=593)	
PSYCHOSOCIAL & MATERIAL SITUATION						
Marital status						<0.001
Married / Cohabiting (%)	89.8	94.3	93.7	89.0	76.4	
Single (%)	7.6	2.9	4.5	8.4	20.2	
Missings (%)	2.6	2.8	1.8	2.6	3.4	
Maternal psychopathology (score)	0.20 (0.25)	0.14 (0.18)	0.18 (0.20)	0.23 (0.28)	0.29 (0.35)	<0.001
Missings (%)	15.0	12.7	11.8	16.6	21.7	
Pregnancy planning						
Planned (%)	77.7	86.4	79.7	75.0	62.0	<0.001
Not planned (%)	18.3	9.9	15.9	21.5	33.5	
Missings (%)	4.0	3.7	4.4	3.5	4.5	
Financial concerns (%)						
No concerns	77.4	89.3	84.9	73.2	49.3	<0.001
Some concerns	9.2	3.6	7.8	11.2	19.4	
Great concerns	1.1	0.2	0.7	1.1	3.7	
Missings (%)	12.2	6.9	6.6	14.5	27.6	
No. in household	2.5 (1.5)	2.6 (0.8)	2.5 (0.7)	2.5 (1.9)	2.7 (2.4)	0.014
Missings (%)	12.7	9.7	9.8	14.1	20.5	
Working hours (hours)	27.2 (13.7)	32.4 (10.9)	27.7 (11.9)	25.1 (14.0)	17.4 (15.9)	<0.001
Missings (%)	13.1	7.8	8.4	16.0	26.1	

TABLE 1. CONTINUED

	TOTAL (N=3546)[b]	LEVEL OF MATERNAL EDUCATION				P-VALUE FOR HETEROGENEITY[a]
		HIGH (N=1162)	MID-HIGH (N=882)	MID-LOW (N=909)	LOW (N=593)	
LIFESTYLE-RELATED FACTORS						
BMI (kg/m²)[c]	24.3 (4.1)	23.4 (3.1)	23.6 (3.3)	25.0 (4.6)	26.0 (5.4)	<0.001
Weight gain (kg)[c]	7.9 (3.6)	7.9 (3.4)	8.2 (3.5)	7.8 (3.8)	7.5 (3.9)	0.003
Missings (%)	3.4	3.2	2.7	3.5	4.4	
Smoking habits						
No (%)	80.5	92.2	86.5	77.0	54.2	<0.001
<5 per day (%)	6.9	3.7	6.7	8.0	12.0	
≥5 per day (%)	8.1	1.2	3.2	10.1	25.8	
Missings (%)	4.5	2.9	3.6	4.8	8.1	
Alcohol consumption					74.9	
No (%)	50.4	32.1	45.4	62.6	14.0	<0.001
<1 drink per week (%)	23.5	29.7	26.4	19.0	9.8	
≥1 drink per week (%)	24.9	36.8	27.7	16.7	1.3	
Missings (%)	1.2	1.4	0.6	1.7		

Values are means (SD) or percentages for total population and by level of maternal education.
[a] ANOVA for continuous variables, $\chi 2$ tests for categorical variables. Tests are performed excluding the missing values of each covariate.
[b] Small numbers of missings on gestational age (n=1), maternal height (n=1), and BMI (n=15).
[c] Adjusted for gestational age at time of the visits.

TABLE 2. BIRTHWEIGHT (GRAMS) CHARACTERISTICS IN THE TOTAL STUDY POPULATION AND BY LEVEL OF MATERNAL EDUCATION [a]

		LEVEL OF MATERNAL EDUCATION				
	TOTAL (N=3546)	HIGH (N=1162)	MID-HIGH (N=882)	MID-LOW (N=909)	LOW (N=593)	OVERALL P-VALUE
Mean birthweight[b]	3540 (496)	3601 (484)	3570 (493)	3506 (501)	3424 (495)	<0.001
Difference in birthweight[c]		0 Reference	-31 [-63, 2]	-94 [-127, -62]	-176 [-216, -136]	<0.001
OR birthweight <2500[d]		1.00 Reference	1.16 [0.67, 3.92]	3.18 [1.46, 6.94]	3.32 [1.44, 7.63]	0.008
OR birthweight >4500[d]		1.00 Reference	0.85 [0.53, 1.39]	0.83 [0.51, 1.34]	0.58 [0.31, 1.09]	0.404

Values are means (SD) or regression coefficients [95% CI]. The regression coefficients reflect the difference in birthweight or odds ratio (OR) relative to the reference group (high education).
[a] All analyses are unadjusted.
[b] ANOVA.
[c] Linear regression analysis.
[d] Logistic regression analyses.

TABLE 3. DIFFERENCES IN BIRTHWEIGHT (G) BY EDUCATIONAL LEVEL AFTER ADJUSTMENT FOR EACH COVARIATE SEPARATELY AND THE CORRESPONDING CHANGE (%) IN BIRTHWEIGHT DIFFERENCES [95% CI] RELATIVE TO THE BASIC MODEL

	DIFFERENCE IN BIRTHWEIGHT (G) BY LEVEL OF MATERNAL EDUCATION			
	HIGH (N=1162)	MID-HIGH (N=882)	MID-LOW (N=909)	LOW (N=593)
Basic model (BM): adjusted for infant gender and gestational age	0 Reference	-20 [-58, 19] g	-60 [-99, -22] g ***	-123 [-167, -79] g ***
PREGNANCY CHARACTERISTICS				
BM + parity	0 Reference	-11 g	-48 g **	-123 ***
Change relative to BM		+ 44 [3, 84] % **	+ 20 [7, 33] %***	0 [-7, 7] %
BM + maternal age	0 Reference	-14 g	-46 g **	-102 g ***
Change compared to BM		+ 27 [5, 48] % **	+ 23 [6, 40] % ***	+ 17 [5, 30] % ***
BM + hypertension	0 Reference	-21 g	-57 g ***	-120 g ***
Change compared to BM		- 5 [-15, 6] %	+ 5 [0, 9] % **	+ 2 [0, 4] %*
ANTHROPOMETRICS				
BM + maternal height	0 Reference	-16 g	-48 g **	-87 g ***
Change relative to BM		+ 16 [-26, 58] %	+ 20 [6, 33] % ***	+ 29 [21, 38] % ***
BM + maternal birthweight	0 Reference	-24 g	-62 g ***	-111 g ***
Change relative to BM		- 23 [-88, 42] %	- 3 [-25, 18] %	+ 10 [-1, 20] % *
BM + paternal height	0 Reference	-8 g	-40 g **	-92 g ***
Change relative to BM		+ 57 [23, 91] % ***	+ 33 [20, 45] %***	+ 25 [17, 33] % ***
BM + paternal birthweight	0 Reference	-14 g	-52 g ***	-109 g ***
Change relative to BM		+ 28 [-19, 74] %	+ 13 [-3, 28] %	+ 11 [2, 21] % **

TABLE 3. CONTINUED

	DIFFERENCE IN BIRTHWEIGHT (g) BY LEVEL OF MATERNAL EDUCATION			
	HIGH (N=1162)	MID-HIGH (N=882)	MID-LOW (N=909)	LOW (N=593)
PSYCHOSOCIAL & MATERIAL SITUATION				
BM + marital status	0 Reference	-18 g	-52 g ***	-98 g ***
Change relative to BM		+ 11 [-6, 28] %	+ 13 [5, 20] %***	+ 20 [12, 28] %***
BM + maternal psychopathology	0 Reference	-19 g	-59 g ***	-120 g ***
Change relative to BM		+ 3 [-10, 17] %	+ 2 [-7, 11] %	+ 2 [-5, 9] %
BM + pregnancy planning	0 Reference	-15 g	-51 g ***	-105 g ***
Change relative to BM		+ 23 [6, 41] % ***	+ 14 [6, 23] % ***	+ 14 [6, 22] %***
BM + financial concerns	0 Reference	-17 g	-54 g ***	-105 g ***
Change relative to BM		+ 15 [0, 29] %**	+ 10 [2, 18] % **	+ 14 [4, 25] % ***
BM + no. in household	0 Reference	-18 g	-59 g ***	-127 g ***
Change relative to BM		+ 10 [-9, 28] %	+ 2 [-4, 7] %	- 4 [-8, -1] % **
BM + working hours	0 Reference	-29 g	-75 g ***	-151 g ***
Change relative to BM		- 49 [-79, 19] % ***	- 25 [-40, -11] % ***	- 25 [-39, 11] % ***
LIFESTYLE-RELATED FACTORS				
BM + BMI	0 Reference	-23 g	-87 g ***	-165 g ***
Change relative to BM		- 16 [-46, 14] %	- 44 [-58, -31] % ***	- 35 [-44, -25] % ***
BM + weight gain	0 Reference	-23 g	-60 g ***	-116 g ***
Change relative to BM		- 19 [-42, 4] % *	+ 1 [-6, 8] %	+ 5 [1, 10] % **
BM + smoking habits	0 Reference	-11 g	-30 g	-42 g
Change relative to BM		+ 45 [11, 79] % **	+ 51 [36, 65] % ***	+ 66 [51, 80] % ***
BM + alcohol consumption	0 Reference	-21 g	-62 g ***	-126 g ***
Change relative to BM		- 5 [-24, 15] %	- 4 [-18, 10] %	- 3 [-12, 7] %

** p-value <0.10, ** p-value <0.05, *** p-value <0.01.*

TABLE 4 shows the educational differences in birthweight after full adjustment for all covariates that independently led to a significant change in the univariate analyses. The differences in birthweight relative to the BM fell by 66% between the highest and lowest educational groups, as is illustrated in FIGURE 1. In the mid-low and mid-high group the differences fell by 45% and 71% respectively. The differences in birthweight between the highest and the other educational groups are statistically non-significant after full adjustment (mid-high: p=0.750; mid-low: p=0.083; low: p=0.097).

TABLE 4. FULL MODEL OF EDUCATIONAL DIFFERENCES IN BIRTHWEIGHT (G) AFTER ADJUSTMENT FOR ALL RELEVANT COVARIATES

VARIABLES	CATEGORIES	REGRESSION COEFFICIENTS	[95% CI]	OVERALL P-VALUE
Intercept		-5533	[-4875, -6192]	‹0.001
Maternal education	High	0	Reference	
	Mid-high	-6	[-41, 30]	
	Mid-low	-33	[-71, 4]	
	Low	-41	[-90, 7]	
Gender	Girl	-117	[-144, -91]	‹0.001
Gestational age		149	[139, 160]	‹0.001
Parity	Primipara	-197	[-229, -164]	‹0.001
Maternal age		-5	[-8, -1]	0.006
Hypertension	Yes	-132	[-184, -145]	‹0.001
Maternal height		12	[9, 14]	‹0.001
Maternal birthweight	›4000 grams	0	Reference	
	3000-4000 grams	-117	[-163, -71]	
	‹3000 grams	-168	[-218, -117]	
Paternal height		6	[5, 8]	‹0.001
Paternal birthweight	›4000 grams	0	Reference	
	3000-4000 grams	-104	[-139, -68]	
	‹3000 grams	-166	[-211, -120]	
Marital status	Single	-15	[-69 ,39]	0.592
Pregnancy planning	Not planned	-9	[-46, 27]	0.620
Financial concerns	No concerns	0	Reference	
	Some concerns	-62	[-106, -17]	
	Great concerns	-53	[-162, 56]	
No. in household		1	[-8, 9]	0.884
Working hours		-0.1	[-1, 1]	0.872
BMI		22	[18, 25]	‹0.001
Weight gain		19	[15, 23]	‹0.001
Smoking habits	No	0	Reference	
	‹5 per day	-139	[-190, -88]	
	≥5 per day	-186	[-235, -137]	

COMPLETE-CASE ANALYSIS

The complete-case sample (n=2028) consisted of 63% of the high educated, 62% of the mid-high educated, 55% of the mid-low educated, and of 41% of the low educated women of the initial study population. Mean birthweight was larger (3578, SD=493) and educational differences in birthweight (difference between high and low education: -100 g, p-value=0.002) were smaller in the complete-case sample than in the total study population. The results of the full model were comparable to the results of the whole study population (45% to 71% explained).

DISCUSSION

While the present study confirmed the presence of inequalities in birthweight, it also showed that these inequalities in birthweight can be understood as the net effect of two opposing influences in pregnant women with a lower education. The first influence is these women's relatively high prevalence of many *risk factors* for lower birthweight: being primipara, younger age, being hypertensive, lower parental height and birthweight, single motherhood, unplanned pregnancy, financial concerns, living in a large household and smoking; the second is their higher prevalence of factors that have a *suppressive effect* on lower birthweight, such as their lower number of working hours and higher BMI. As the first tendency is stronger than the second, lower educated women give birth to infants with a lower mean birthweight. A large part of the differences in birthweight between the highest and the other educational groups was explained (45%-71%) while taking both influences into account.

COMPARISON WITH OTHER STUDIES

The extent of the unadjusted educational differences in birthweight we report is comparable with that contained in the available literature on socioeconomic inequalities in birthweight.[7-10 15-18] Despite its abundance of covariates in the explanatory models, our study resulted in only a slightly higher percentage of explained educational differences in birthweight than earlier studies did with only a few explanatory variables.[14-17] This is probably a consequence of the fact that our fully adjusted model simultaneously included risk factors and suppressive factors for a relatively low birthweight among lower educated women.

EXPLANATION OF EDUCATIONAL INEQUALITIES IN BIRTHWEIGHT

In our study, parity, age, and height of the pregnant women, hypertension, marital status, and smoking habits explained important parts of the association between educational level and birthweight, which confirms previous reports.[14-17] Of all studied factors, smoking habits of pregnant women explained by far the largest part of the educational differences in birthweight. The explained part of 45% to 66% by adjusting for smoking is comparable with Finnish research showing that smoking explained up to half the excess risk for low birthweight in the lowest socioeconomic group.[14] Unlike earlier studies, we also examined parental birthweight, paternal height and psychosocial characteristics as possible explanatory factors; these variables indeed explained a statistically significant part of the association.

High parental birthweight and height can be considered as a proxy of a genetic predisposition for a relatively high birthweight of the offspring.[19] The literature on the effects of prenatal stress shows that circumstances such as single motherhood, unplanned pregnancy, financial concerns and living in more crowded households are associated with a relatively high risk of having a low birthweight infant, which is attributed to a pregnant woman's physiological and hormonal responses to stress.[21 22] Since these adverse situations were more prevalent among the lower

educated women in our study, we hypothesize that psychosocial factors contribute to the existence of educational inequalities in birthweight through stress and its associated physical responses.

The present study showed that lower educated pregnant women also have a relatively high prevalence of certain factors that have a suppressive effect on low birthweight. First, these women have a higher mean BMI, which is positively correlated with birthweight.[19] However, a high BMI during pregnancy is associated with a greater risk of pre-eclampsia and gestational diabetes,[39] which can create several health risks for the unborn child, including birth trauma, induced preterm delivery, macrosomia and even neonatal death.[40 41] Thus, despite the suppressive effect of BMI on low birthweight among women with a lower education, high BMI represents risks to a pregnant woman and her unborn child, and is therefore not recommended.

The second factor with a suppressive effect was the lower number of hours worked by lower educated pregnant women. This number was inversely associated with birthweight (data not shown), which explains the increasing birthweight differences between the different educational groups when adjusting for working hours. Further research should establish whether the number of working hours per week is causally related to birthweight and other pregnancy outcomes, an association on which the available literature has reported inconsistent findings.[42-44]

STRENGTHS AND LIMITATIONS OF THE STUDY

The strengths of the present study are the large number of participating pregnant women with different levels of education, its prospective population-based design and the detailed information on numerous explanatory variables[19 21 32]. Additionally, unlike studies that have focused only on clinically low birthweight, we analyzed differences across the whole continuum of birthweight. Finally, a thorough missing values procedure was applied to our data. The complete case analysis indicated that among lower educated women those with a higher birthweight of the offspring respond better than those with a lower birthweight. We decided to impute missing data instead of excluding those with missing values, as multiple imputation has the benefit of circumventing these selection mechanisms involved in missing values. Moreover, using multiple imputation instead of complete case analysis also increased statistical power due to a larger study population.

Some methodological issues also need to be considered. Sixty-eight percent of all infants born to Dutch women in the study area were participants in the Generation R Study. Because women and infants in the overall Generation R cohort have a lower prevalence of medical complications than the prevalence projected in population figures in Rotterdam,[28 30] participants in the present study probably represent a selection towards a more healthy population.

Furthermore, information on many covariates in this study was self-reported, which may have resulted in underreporting of smoking and alcohol consumption. These misclassifications are probably not random. For instance, studies among young adults[45] and pregnant women[46] demonstrated that cigarette smoking was

significantly underreported in those who were low educated. Consequently, the effect sizes and thereby possibly the explained part of educational differences in birthweight by smoking and alcohol consumption may be underestimated. Other covariates such as parental birthweight may have been subject to recall bias. Such a bias would presumably be random; we are unaware whether it influenced the effect estimates, or how.

As some determinants of birthweight were not available for this study, we were unable to take into account all possible explanatory factors. For instance, data on maternal dietary intake were not yet available at the time this study was conducted. Pregnant women need additional energy intake (approximately 300 kcal per day) to achieve optimal fetal growth; this is especially recommended during the second and third trimester of pregnancy.[32] Furthermore, studies showed beneficial effects on birthweight of protein, vitamin, and omega-3 fatty acids intake.[22 32] Research among pregnant women has indicated that socioeconomic status was positively associated with fruit, vegetable and fish consumption and inversely related to intake of high-fat foods.[47-49] Therefore, including dietary patterns in our study may result in different estimates of the full-adjusted model and possibly leads to a somewhat larger proportion explained birthweight differences.

Finally, the use of regression adjustment to assess mediation has been criticized, since the required assumptions on causality are difficult to verify and the percentage change can be similar for different absolute changes in effect estimates.[50] The latter issue could partially be solved by expressing estimates in standard deviation scores, but this would make interpretation of the regression coefficients less comprehensible. So, as alternative methods are not necessarily better, regression adjustment remains a widely used approach to investigate the contribution of risk factors to SES differences in health.

IMPLICATIONS OF THE STUDY

Reducing socioeconomic inequalities in birthweight is an important public health issue, since such inequalities may be precursors of the socioeconomic gradient in health throughout life.[10 13] Generally, a higher birthweight is associated with better health conditions.[1-6] However, Graafmans et al[51] reported a U-shaped relation between birthweight and perinatal mortality: relatively low birthweights and relatively high birthweights both being associated with an increased risk of mortality. Although statistically non-significant, the risk of macrosomia was slightly higher among higher educated pregnant women in the present study. Given the associated health risks, it is important to monitor whether the association between educational level and macrosomia is confirmed in other studies. The results of such a study will indicate whether interventions are needed to prevent macrosomia among women in higher socioeconomic strata.

Some of the covariates that explained part of the educational inequalities in birthweight seem to be modifiable by intervention programs. Altering smoking habits may be an option to reduce educational differences in birthweight, as a relatively high percentage (38%) of lower educated women continued to smoke during

pregnancy as compared the highest educated women (5%). Prenatal care providers must be aware that especially women with a lower education tend to continue smoking during pregnancy. They should apply evidence-based intervention strategies to get pregnant women to stop smoking.[52] Additionally, nationwide campaigns could raise awareness about the detrimental effects of smoking on maternal and fetal health.

It is also desirable but potentially more difficult to change the educational gradient in other factors. For instance, the prevalence of hypertension might be lowered by calcium supplementation and low-dose aspirin treatment among women at risk for hypertensive complications during pregnancy.[53] Furthermore, we recommend the development and implementation of effective strategies for preventing adverse circumstances in pregnant women, such as single motherhood, having financial concerns and unplanned pregnancies. Since initiation of prevention programs during pregnancy may be too late, the most effective strategy is probably by embedding these programs in preconception care.[54] In order to tackle inequalities in birthweight, it is of crucial importance that effective interventions are accessible for pregnant women in the lower socioeconomic strata.

In conclusion, our study confirmed remarkable educational inequalities in birthweight, which were largely explained by pregnancy characteristics, anthropometrics, psychosocial and material situation, and lifestyle-related factors. To unravel the whole spectrum of causes of the inequalities we have reported here, further research remains necessary. In the meantime, effective public health interventions should be developed and implemented to reduce undesirable socioeconomic inequalities in birthweight.

REFERENCES

1. Alexander GR, Kogan M, Bader D, Carlo W, Allen M, Mor J. US birth weight/gestational age-specific neonatal mortality: 1995-1997 rates for whites, hispanics, and blacks. *Pediatrics.* 2003;111(1):e61-6.
2. Wilcox AJ, Skjaerven R. Birth weight and perinatal mortality: the effect of gestational age. *Am J Public Health.* 1992;82(3):378-82.
3. Barker DJP. *Mothers, babies and health in later life*. Edinburgh, UK: Churchill Livingston, 1998.
4. Lawlor DA, Ronalds G, Clark H, Smith GD, Leon DA. Birth weight is inversely associated with incident coronary heart disease and stroke among individuals born in the 1950s: findings from the Aberdeen Children of the 1950s prospective cohort study. *Circulation.* 2005;112(10):1414-8.
5. Gale CR, Martyn CN. Birth weight and later risk of depression in a national birth cohort. *Br J Psychiatry.* 2004;184:28-33.
6. Wahlbeck K, Forsen T, Osmond C, Barker DJ, Eriksson JG. Association of schizophrenia with low maternal body mass index, small size at birth, and thinness during childhood. *Arch Gen Psychiatry.* 2001;58(1):48-52.
7. Koupilova I, Bobak M, Holcik J, Pikhart H, Leon DA. Increasing social variation in birth outcomes in the Czech Republic after 1989. *Am J Public Health.* 1998;88(9):1343-7.
8. Luo ZC, Kierans WJ, Wilkins R, Liston RM, Mohamed J, Kramer MS. Disparities in birth outcomes by neighborhood income: temporal trends in rural and urban areas, british columbia. *Epidemiol.* 2004;15(6):679-86.
9. Mackenbach JP. Socio-economic health differences in The Netherlands: a review of recent empirical findings. *Soc Sci Med.* 1992;34(3):213-26.
10. Moser K, Li L, Power C. Social inequalities in low birth weight in England and Wales: trends and implications for future population health. *J Epidemiol Community Health.* 2003;57(9):687-91.
11. Huisman M, Kunst AE, Bopp M, Borgan JK, Borrell C, Costa G, et al. Educational inequalities in cause-specific mortality in middle-aged and older men and women in eight western European populations. *Lancet.* 2005;365(9458):493-500.
12. Smith GD, Bartley M, Blane D. The Black report on socioeconomic inequalities in health 10 years on. *BMJ.* 1990;301(6748):373-7.
13. Spencer N, Logan S. Social influences on birth weight. *Arch Dis Child Fetal Neonatal Ed.* 2002;86(1):F6-7.
14. Gissler M, Merilainen J, Vuori E, Hemminki E. Register based monitoring shows decreasing socioeconomic differences in Finnish perinatal health. *J Epidemiol Community Health.* 2003;57(6):433-9.
15. Koupilova I, Rahu K, Rahu M, Karro H, Leon DA. Social determinants of birthweight and length of gestation in Estonia during the transition to democracy. *Int J Epidemiol.* 2000;29(1):118-24.
16. Raum E, Arabin B, Schlaud M, Walter U, Schwartz FW. The impact of maternal education on intrauterine growth: a comparison of former West and East Germany. *Int J Epidemiol.* 2001;30(1):81-7.
17. Reime B, Ratner PA, Tomaselli-Reime SN, Kelly A, Schuecking BA, Wenzlaff P. The role of mediating factors in the association between social deprivation and low birth weight in Germany. *Soc Sci Med.* 2006;62(7):1731-44.
18. Wilcox MA, Smith SJ, Johnson IR, Maynard PV, Chilvers CE. The effect of social deprivation on birthweight, excluding physiological and pathological effects. *BJOG.* 1995;102(11):918-24.
19. Kramer MS. Intrauterine growth and gestational duration determinants. *Pediatrics.* 1987;80(4):502-11.

20. Andersson SW, Niklasson A, Lapidus L, Hallberg L, Bengtsson C, Hulthen L. Sociodemographic characteristics influencing birth outcome in Sweden, 1908-1930. Birth variables in the Population Study of Women in Gothenburg. *J Epidemiol Community Health* 2000;54(4):269-78.
21. Mulder EJ, Robles de Medina PG, Huizink AC, Van den Bergh BR, Buitelaar JK, Visser GH. Prenatal maternal stress: effects on pregnancy and the (unborn) child. *Early Hum Dev.* 2002;70(1-2):3-14.
22. Hobel C, Culhane J. Role of psychosocial and nutritional stress on poor pregnancy outcome. *J Nutr.* 2003;133(5 Suppl 2):1709S-1717S.
23. Hobcraft J. Women's education, child welfare and child survival: a review of the evidence. *Health Transit Rev.* 1993;3(2):159-75.
24. Woods R, Watterson P, Woodward J. The causes of Rapid Infant Mortality Decline in England and Wales, 1861-1921. Part II. *Popul Stud.* 1989;43(1):113-132.
25. Savitz DA, Kaufman JS, Dole N, Siega-Riz AM, Thorp JM, Jr., Kaczor DT. Poverty, education, race, and pregnancy outcome. *Ethn Dis.* 2004;14(3):322-9.
26. Shmueli A, Cullen MR. Birth weight, maternal age, and education: new observations from Connecticut and Virginia. *Yale J Biol Med.* 1999;72(4):245-58.
27. Hofman A, Jaddoe VW, Mackenbach JP, Moll HA, Snijders RF, Steegers EA, et al. Growth, development and health from early fetal life until young adulthood: the Generation R Study. *Paediatr Perinat Epidemiol.* 2004;18(1):61-72.
28. Jaddoe VW, Mackenbach JP, Moll HA, Steegers EA, Tiemeier H, Verhulst FC, et al. The Generation R Study: Design and cohort profile. *Eur J Epidemiol.* 2006;21(6):475-84.
29. Alexander GR, Kogan M, Martin J, Papiernik E. What are the fetal growth patterns of singletons, twins, and triplets in the United States? *Clin Obstet Gynecol.* 1998;41(1):114-25.
30. Center for Research and Statistics, Rotterdam (COS). http://www.cos.rotterdam.nl. 2005.
31. Statistics Netherlands. Standaard Onderwijsindeling 2003. Voorburg/Heerlen. 2004a.
32. Valero De Bernabe J, Soriano T, Albaladejo R, Juarranz M, Calle ME, Martinez D, et al. Risk factors for low birth weight: a review. *Eur J Obstet Gynecol Reprod Biol.* 2004;116(1):3-15.
33. Verburg BO, Steegers EAP, Ridder MAd, Snijders RJM, Hofman A, Moll HA, et al. New charts for ultrasound dating of pregnancy and assessment of fetal growth: longitudinal data from a population-based cohort study. *Ultrasound Obstet Gynecol.* 2007;In press.
34. Derogatis LR. *Brief Symptom Inventory (BSI): Administration, scoring and procedures. Manual, third edition*. Minneapolis, MN, USA, 1993.
35. de Beurs E. *Brief Symptom Inventory.* Handleiding, Leiden, The Netherlands, 2004.
36. MacKinnon D. Contrasts in multiple mediator models. In: Rose JS, Chassin L, Presson CC, Shermon SJ, editors. *Multivariate Applications in Substance Use Research: New Methods for Nem Questions*. Mahwah, NJ: Lawrence Erlbaum, 2000:141-160.
37. Efron B, Tibshirani RJ. *An Introduction to the Bootstrap*. London, UK: Chapman and Hall, 1993.
38. Harrell Jr. FE. *Regression Modeling Strategies: With Applications to Linear Models, Logistics Regression, and Survival Analysis*. New York, USA: Springer-Verlag New York, Inc., 2001.
39. Yu CK, Teoh TG, Robinson S. Obesity in pregnancy. *BJOG.* 2006;113(10):1117-25.
40. Basso O, Rasmussen S, Weinberg CR, Wilcox AJ, Irgens LM, Skjaerven R. Trends in fetal and infant survival following preeclampsia. *JAMA.* 2006;296(11):1357-62.
41. Kwik M, Seeho SK, Smith C, McElduff A, Morris JM. Outcomes of pregnancies affected by impaired glucose tolerance. *Diabetes Res Clin Pract.* 2007;77(2):263-8.
42. Bonzini M, Coggon D, Palmer KT. Risk of prematurity, low birthweight and pre-eclampsia in relation to working hours and physical activities: a systematic review. *Occup Environ Med.* 2007;64(4):228-43.

43. Peoples-Sheps MD, Siegel E, Suchindran CM, Origasa H, Ware A, Barakat A. Characteristics of maternal employment during pregnancy: effects on low birthweight. *Am J Public Health.* 1991;81(8):1007-12.

44. Simpson JL. Are physical activity and employment related to preterm birth and low birth weight? *Am J Obstet Gynecol.* 1993;168(4):1231-8.

45. Wagenknecht LE, Burke GL, Perkins LL, Haley NJ, Friedman GD. Misclassification of smoking status in the CARDIA study: a comparison of self-report with serum cotinine levels. *Am J Public Health* 1992;82(1):33-6.

46. Parna K, Rahu M, Youngman LD, Rahu K, Nygard-Kibur M, Koupil I. Self-reported and serum cotinine-validated smoking in pregnant women in Estonia. *Matern Child Health J* 2005;9(4):385-92.

47. Erkkola M, Karppinen M, Jarvinen A, Knip M, Virtanen SM. Folate, vitamin D, and iron intakes are low among pregnant Finnish women. *Eur J Clin Nutr* 1998;52(10):742-8.

48. Whichelow MJ, Prevost AT. Dietary patterns and their associations with demographic, lifestyle and health variables in a random sample of British adults. *Br J Nutr.* 1996;76(1):17-30.

49. Rogers I, Emmett P, Baker D, Golding J. Financial difficulties, smoking habits, composition of the diet and birthweight in a population of pregnant women in the South West of England. ALSPAC Study Team. Avon Longitudinal Study of Pregnancy and Childhood. *Eur J Clin Nutr* 1998;52(4):251-60.

50. Kaufman JS, Maclehose RF, Kaufman S. A further critique of the analytic strategy of adjusting for covariates to identify biologic mediation. *Epidemiol Perspect Innov* 2004;1(1):4.

51. Graafmans WC, Richardus JH, Borsboom GJ, Bakketeig L, Langhoff-Roos J, Bergsjo P, et al. Birth weight and perinatal mortality: a comparison of "optimal" birth weight in seven Western European countries. *Epidemiology.* 2002;13(5):569-74.

52. Melvin CL, Dolan-Mullen P, Windsor RA, Whiteside HP, Jr., Goldenberg RL. Recommended cessation counselling for pregnant women who smoke: a review of the evidence. *Tob Control.* 2000;9 Suppl 3:III80-4.

53. Sibai B, Dekker G, Kupferminc M. Pre-eclampsia. *Lancet* 2005;365(9461):785-99.

54. Weerd S, Steegers E. The past and present practices and continuing controversies of preconception care. *Community Genet.* 2002;5(1):50-60.

CHAPTER **2.4**

Employment status and the risk of pregnancy complications

ABSTRACT

OBJECTIVES: The association between employment status during pregnancy and pregnancy outcome remains unclear. Therefore this study explored the relation between employment status, type of unemployment and number of weekly working hours, with a wide range of pregnancy outcomes.

METHODS: The study was embedded within a population-based cohort study in the Netherlands. Information on employment characteristics and pregnancy outcomes was available for 6111 pregnant women.

RESULTS: After adjustment for confounders, there were no statistically significant differences in risks of pregnancy complications between employed and unemployed women. In the subgroup of unemployed women, women receiving disability benefit had an increased risk of preterm ruptured membranes (OR=3.16, 95% CI: 1.49, 6.70), elective caesarean section (OR=2.98, 95% CI: 1.21, 7.34), and preterm birth (OR=2.64, 95% CI: 1.32, 5.28) as compared to housewives. Offspring of both students and women receiving disability benefit had a significantly lower mean birth weight than the offspring of housewives (difference: -93, 95% CI: -174, -12; and -97, 95% CI: -190, -5, respectively). In the subgroup of employed women, long working hours (i.e. ≥40 h/week) were associated with a decrease of 54 g in offspring's mean birth weight (adjusted analysis; 95% CI: -89, -1) compared with 1 to 24 h/weekly working hours.

CONCLUSIONS: We found no indications that paid employment during pregnancy benefits or endangers the health of mother and child. Within the subgroups of unemployed and employed women we observed, however, that women receiving disability benefit, students and women with long working hours during pregnancy were at risk for some adverse pregnancy outcomes. More research is needed to replicate these results and to provide explanations for these findings. Meanwhile, prenatal care providers should be made aware of the risks associated with specific types of unemployment and long working hours.

INTRODUCTION

The employment rate of women is increasing in many Western countries. In the European Union the proportion of employed women increased from about 50% in 1997 to 60% in 2007;[1] this implies a growing number of women who work during their pregnancy. Studies in the general population show that paid employment is associated with a better health status as compared to being unemployed;[2-4] this phenomenon is called the 'healthy worker effect'.[5] This raises the question whether there is also a positive association between paid employment and pregnancy outcomes, or whether there are unfavourable effects of paid employment regarding pregnancy outcomes due to, for example, overload.

Earlier research on employment status during pregnancy was primarily aimed at exploring the relation between paid employment (present versus absent) with gestational duration and birth weight; however, due to inconsistent findings the direction and magnitude of this association remains unclear.[6-11] Whether paid employment is related to other indicators of neonatal health, maternal pregnancy complications, and/or delivery characteristics remains largely unknown, as research in this area is lacking.

Besides comparing pregnancy outcomes of employed and unemployed women, the effect of long weekly working hours on pregnancy outcomes among employed women has also been investigated. It was consistently reported that there is no association between the number of weekly working hours and the risk of low birth weight;[8 9 12 13] however, for preterm birth inconsistent findings were reported.[8-11 13 14] The relation between weekly working hours and pregnancy outcomes other than gestational duration and birth weight has seldom been explored. A study in the USA indicated that pregnant women with gestational hypertension worked more hours per week than the control group;[15] Hung and colleagues found no association between the weekly working hours of pregnant women and the risk of caesarean delivery.[16] Although several studies focused on employment characteristics (e.g. the working hours of employed women), the group of unemployed women was seldom examined in more detail. Therefore, it remains unknown whether all unemployed women have the same risk of pregnancy complications, or whether this comprises a more heterogeneous group.

The present study examined the relation between employment status during pregnancy and a wide range of pregnancy outcomes, such as maternal pregnancy complications, delivery outcomes and markers of neonatal health. Among unemployed pregnant women, we explored whether specific types of unemployment (house wife, job-seeking / receiving basic social security benefit, receiving disability benefit, and student) are associated with pregnancy outcomes. For employed pregnant women, the relation between the number of weekly working hours and pregnancy outcomes was examined. For this, we used data from the Generation R Study, a large prospective birth-cohort study in the Netherlands.

METHODS

DESIGN

This study was embedded in the Generation R Study, a population-based cohort study from foetal life onwards; this is described in detail elsewhere.[17 18] All pregnant women living in the study area (Rotterdam, the Netherlands) were informed about the study by healthcare workers (e.g. community midwives and obstetricians). In total, 8880 pregnant women of different ethnicities with a delivery date between April 2002 and January 2006 enrolled in the prenatal part of the study. Of all pregnant women in the study area that had a live birth, 61% participated in the Generation R Study (based on cohort years 2003 and 2004: of the 8494 live births, 5189 participated). Assessments, including physical examinations, foetal ultrasound examinations, and questionnaires, were planned in early (5-18 weeks' gestation; median=13 weeks), mid- (18-25 weeks' gestation; median=20 weeks) and late pregnancy (25-39 weeks' gestation; median=30 weeks). Written informed consent was obtained from all participants. The local Medical Ethical Committee approved the study.

POPULATION FOR ANALYSIS

Of the 8880 participants who enrolled in the Generation R Study during pregnancy, those who had had a miscarriage (n=78), induced abortion (n=29), twin pregnancy (n=93), as well as those who enrolled in the study after 25 weeks' gestation (n=350) were excluded from the present study. Additionally, we excluded women without information on employment status (n=2219), yielding a sample size of 6111 pregnant women for the present analyses. Because data on one or more of the pregnancy complications were missing for some of the participants, the population for analyses varied per outcome (n between 5585 and 6110).

EMPLOYMENT STATUS AND WEEKLY WORKING HOURS

Information on employment during pregnancy was obtained by postal questionnaire in late pregnancy (≥25 weeks' gestation). The women were asked to fill out which of the following descriptions applied most to them at that moment: paid employment, self-employed, job-seeking / receiving basic social security benefit, receiving disability benefit, housewife, or student. We generated the dichotomous variable 'employment status' by combining the first two categories ('paid employment') and merging the remaining categories ('unemployed'). The number of weekly working hours of the participants with paid employment was assessed by means of the open question "*How many hours per week do you work?*" Working hours were categorized into '1-24', '25-39', and '40 or more hours a week'.

PREGNANCY COMPLICATIONS

Information on the following pregnancy complications was obtained from the medical records and delivery reports of the hospital and midwife registries (complications indicated in *italics*):

- *Pregnancy-induced hypertension and pre-eclampsia* were defined according to the criteria described by the International Society for the Study of Hypertension in Pregnancy.[19] Pregnancy-induced hypertension was diagnosed if previously normotensive women had a systolic blood pressure of at least 140 mmHg and/or a diastolic blood pressure of at least 90 mmHg after 20 weeks of gestation; if pregnant women additionally had proteinuria (≥300 mg/24 h), then they were diagnosed as pre-eclamptic.
- *Gestational diabetes* was diagnosed according to Dutch midwifery and obstetric guidelines using the following criteria: random glucose level above 11.1 mmol/l or a glucose level higher than 7.0 mmol/l after fasting, without previously diagnosed diabetes.
- *Preterm ruptured membranes* before 37 weeks' gestation were defined as present ('yes') or absent ('no').
- *Poor progress of delivery* was defined as failure to progress during the first and/or second stage of labour (yes/no).
- *Mode of delivery* was categorized as 'spontaneous delivery', 'assisted vaginal delivery', 'elective caesarean section', and 'emergency caesarean section'.
- We determined gestational age by foetal ultrasound examination at the first visit to our research centre. Pregnancy dating curves were constructed using subjects for whom we had both ultrasound examinations <25 weeks' gestation and reliable information on last menstrual period.[20] Subsequently, all pregnancies in our study were dated using these curves. *Birth* was classified as *preterm* if it occurred at <37 weeks' gestation.
- *Meconium-stained amniotic fluid* was defined as present ('yes') or absent ('no').
- We dichotomized the continuous *Apgar score at 5 minutes* into <7 or ≥7.
- *Birth weight* was measured in grams.
- *Small-for-gestational-age* (SGA) was based on gestational age and gender specific birth weight distributions. Babies were defined as SGA if they were below the 10th percentile.[21]

CONFOUNDERS

The following variables were considered as possible confounders in the association between employment characteristics and pregnancy outcomes. Age, height and weight of the pregnant women were assessed at enrolment. Body mass index (BMI) was calculated (kg/m^2). A questionnaire was used to obtain information on ethnicity (Dutch, other Western, non-Western), educational level (low, high), family income (<2000 and >2000 euros per month), marital status (married/cohabiting, single), smoking and alcohol consumption during pregnancy, and parity. Smoking was categorized as: no smoking, <5 cigarettes per day and ≥5 cigarettes per day. Alcohol consumption was categorized according to the amount of alcoholic con-

sumptions per week: no drinking, <1 drink per week, 1-6 drinks per week, and ≥1 drinks per day. Due to the small numbers, the latter two categories were merged in the multivariate analyses. We defined parity as the number of live births the participants had previously delivered (0, ≥1). Maternal psychopathology was assessed using the Brief Symptom Inventory, a validated self-report;[22] the weighted sum score of the 53 items indicates the global severity of psychopathological symptoms, with higher scores denoting more symptoms. Information on the gender of the offspring was obtained from the hospital and midwife registries.

STATISTICAL ANALYSES

Univariate logistic regression was used to calculate odds ratios (ORs) for pregnancy complications among employed participants as compared to the reference group of unemployed pregnant women. Subsequently, in multivariate logistic regression analyses the ORs were adjusted for potential confounding factors. For birth weight (a continuous outcome) linear regression was applied; the multivariate linear regression analysis was also adjusted for gestational age at birth. Next, in the subgroup of unemployed women, we calculated adjusted ORs for pregnancy complications per subgroup of unemployment (job seeking, receiving disability benefit, student) as compared to the reference group of housewives. Finally, among participants with paid employment during pregnancy, logistic regression was applied to examine the adjusted association between weekly working hours and pregnancy outcomes; again, linear regression was applied for birth weight. To test for trends, we replicated the latter analyses including weekly working hours as a continuous variable. In the multivariate analyses, missing values on confounders were replaced by the median (categorical variables, BMI, and psychopathological symptoms) or the mean (age). All statistical analyses were performed using the Statistical Package of Social Sciences version 11.0 for Windows (SPSS Inc, Chicago, IL, USA).

NON-RESPONSE ANALYSES

Women with missing data on employment status (n=2219) were compared with women who filled out the questions on employment (n=6111). Data on employment status was relatively more often missing in pregnant women who were younger (F-test=67; df=1; p<0.001), lower educated (χ^2=398; df=1; p<0.001), of non-Western origin (χ^2=296; df=1; p<0.001), single (χ^2=160; df=1; p<0.001), and in those who smoked (χ^2=14; df=1; p<0.001) as compared to women who filled out the questions on employment. Women with missing data more often had a preterm birth (χ^2=8; df=1; p=0.004), an Apgar score below 7 at 5 minutes (χ^2=8; df=1; p=0.004), and a lower birth weight of the offspring (F-test=63; df=1; p<0.001). Women with and without data on employment status did not differ with regard to the prevalence of pre-eclampsia (χ^2=1.3; df=1; p=0.259), meconium stained amniotic fluid (χ^2=0,4; df=1; p=0.529), and caesarean section (elective: χ^2=2.4; df=1; p=0.122; emergency: χ^2=0.2; df=1; p=0.679).

RESULTS

The characteristics of the pregnant women according to their employment status are presented in TABLE 1. Of all participants, 28% (n=1703) was unemployed and 72% (n=4408) reported to have paid work. The unemployed women were younger (F=598; df=1; p<0.001), lower educated (χ^2=650; df=1; p<0.001), and more often of non-Western origin (χ^2-=814; df=1; p<0.001) compared with women with paid employment. Unemployed women were also more often single (χ^2=229; df=1; p<0.001) and reported more psychopathological symptoms (χ^2-=329; df=1; p<0.001). Employed women were more often nulliparous than unemployed women (χ^2=116; df=1; p<0.001).

TABLE 1. CHARACTERISTICS OF THE PREGNANT WOMEN ACCORDING TO THEIR EMPLOYMENT STATUS

			EMPLOYMENT STATUS	
	Nº	TOTAL (N=6111)	UNEMPLOYED (N=1703)	EMPLOYED (N=4408)
Age (years)	6111	30.2 (5.0)	27.8 (5.6)	31.1 (4.5) **
Parity (% nulli)	6040	57.4	47.1	62.3 **
Educational level (% low)	5840	51.7	79.9	42.4 **
Family income (% <2000 euro)	5637	36.1	67.6	20.0 **
Ethnicity: Dutch (%)	3324	56.3	28.4	65.7 **
Other Western (%)	713	12.1	11.0	12.5 **
Non-Western (%)	1867	31.6	60.7	21.8 **
Marital status (% single)	5802	11.5	22.6	8.1 **
Smoking during pregnancy: No smoking (% yes)	4725	77.4	72.5	79.3 ***
<5 cigarettes a day (% yes)	702	11.5	13.2	10.8 ***
≥5 cigarettes a day (% yes)	681	11.1	14.4	9.9 ***
Drinking during pregnancy: No drinking (% yes)	2745	45.9	64.8	38.8 ***
<1 drink per week (% yes)	1769	29.6	22.1	32.4 ***
1-6 drinks per week (% yes)	1272	21.3	11.2	25.1 ***
≥1 drinks per day (% yes)	194	3.2	2.0	3.7 ***
BMI (kg/m²)	6069	23.7 (15.3–50.8)	24.0 (15.6–50.8)	23.6 (15.3–49.4) **
Psychopathology (score)#	5358	0.15 (0.00–3.04)	0.24 (0.00–3.04)	0.13 (0.00–2.86) **
Gender of the offspring (% boys)	6106	50.3	50.6	50.3

Values are percentages for categorical variables, mean (SD) for age, and median (100% range) for BMI and psychopathology
 # Measured with the Brief Symptom Inventory
º Data were missing on parity (n=71), education (n=271), income (n=474), ethnicity (n=207), marital status (n=309), smoking (n=3) and drinking during pregnancy (n=131), BMI (n=42), psychopathology (n=753), offspring's gender (n=5)
** p-value <0.05*
*** <0.001 for employed versus unemployed using c2-tests for categorical variables, ANOVA for age, and Kruskal-Wallis test for BMI and psychopathology.*

Several different pregnancy complications were studied. Of all 6111 women, 3129 had no complications, 1546 had one of these complications, 1050 had two complications, and 286 had three or more complications. Table 2 presents the association between the employment status of the participants and pregnancy complications. None of these associations remained statistically significant after adjustment for the confounders. The unadjusted decreased risks of preterm ruptured membranes (OR=0.71, 95% CI: 0.54, 0.95), preterm birth (OR=0.73, 95% CI: 0.57, 0.94), meconium-stained amniotic fluid (OR=0.85, 95% CI: 0.73, 0.99), and small-for-gestational-age (OR=0.78, 95% CI: 0.65, 0.93) among employed women attenuated to statistical non-significance in the adjusted analyses due to a combination of confounders, mainly family income, educational level, ethnicity, marital status, and psychopathology of the women (data not shown). The unadjusted elevated risks of poor progress of delivery (OR=1.49, 95% CI: 1.26, 1.76) and non-spontaneous delivery (assisted vaginal delivery: OR=2.04, 95% CI: 1.71, 2.44; elective caesarean delivery: OR=1.72, 95% CI: 1.27, 2.33; emergency caesarean delivery: OR=1.26, 95% CI: 1.01, 1.58) in the employed group were also no longer statistically significant in the adjusted analyses; this was largely due to the primiparity of these women.

Several women (n=159) indicated that they had stopped working during pregnancy due to pregnancy related problems. Of these women, 84 were classified as unemployed and 75 as employed. To estimate whether this has influenced our results, we excluded these 159 women and then repeated the analyses on the association between employment status and pregnancy complications. The ORs and levels of statistical significance were similar before and after exclusion of women who had stopped working during pregnancy, indicating that this specific group did not bias our results.

TABLE 3A shows the adjusted ORs for adverse pregnancy outcomes per type of unemployment as compared to paid employment. Housewives and job-seeking women had the same risk of adverse pregnancy outcomes as employed women. Women receiving disability benefit had an elevated risk of pregnancy induced hypertension (OR=2.22, 95% CI: 1.00, 4.91) and preterm birth (OR=2.35, 95% CI: 1.28, 4.31) as compared to employed women. Offspring of women receiving disability benefit and of students had a four-times increased risk of an Apgar score below 7 at 5 minutes after birth (OR=4.19, 95% CI: 1.48, 11.9; and OR=3.71, 95% CI: 1.36, 10.1, respectively).

In TABLE 3B the adjusted risks of adverse pregnancy outcomes per type of unemployment as compared to housewives are presented. Job-seeking women had a higher risk of pre-eclampsia (OR=2.54, 95% CI: 1.03, 6.26) than housewives. Women receiving disability benefit were more likely to have preterm ruptured membranes (OR=3.16, 95% CI: 1.49, 6.70), elective caesarean section (OR=2.98, 95% CI: 1.21, 7.34), and preterm birth (OR=2.64, 95% CI: 1.32, 5.28) than housewives. The offspring of students and of women receiving disability benefit had a significantly lower mean birth weight than the offspring of housewives (difference: -93, 95% CI: -174, -12; and -97, 95% CI: -190, -5, respectively).

TABLE 2. ASSOCIATION BETWEEN EMPLOYMENT STATUS OF PREGNANT WOMEN AND PREGNANCY OUTCOMES

PREGNANCY OUTCOMES	N		OR FOR ADVERSE PREGNANCY OUTCOME (95% CI)		
	OVERALL	CASES	UNEMPLOYED (N=1703)	PAID EMPLOYMENT (N=4408)	PAID EMPLOYMENT (N=4408)
				Unadjusted	Adjusted[#]
Pregnancy-induced hypertension	5994	239	Reference	1.18 (0.88, 1.60)	0.73 (0.50, 1.05)
Pre-eclampsia	5994	126	Reference	0.96 (0.65, 1.42)	0.96 (0.60, 1.53)
Gestational diabetes	5898	66	Reference	1.20 (0.68, 2.12)	1.84 (0.95, 3.54)
Preterm ruptured membranes	5891	222	Reference	**0.71 (0.54, 0.95)**	0.78 (0.55, 1.09)
Poor progress of delivery	5888	952	Reference	**1.49 (1.26, 1.76)**	1.06 (0.87, 1.30)
Mode of delivery	5585				
Assisted vaginal delivery[¶]		969	Reference	**2.04 (1.71, 2.44)**	1.23 (0.96, 1.53)
Elective caesarean delivery[¶]		268	Reference	**1.72 (1.27, 2.33)**	1.18 (0.83, 1.69)
Emergency caesarean delivery[¶]		442	Reference	**1.26 (1.01, 1.58)**	0.84 (0.64, 1.11)
Preterm birth (<37 weeks)	6110	292	Reference	**0.73 (0.57, 0.94)**	0.79 (0.59, 1.07)
Meconium-stained amniotic fluid	5833	901	Reference	**0.85 (0.73, 0.99)**	0.87 (0.72, 1.05)
Apgar score at 5 minutes (<7)	5907	63	Reference	0.62 (0.37, 1.03)	0.56 (0.30, 1.04)
Small-for-gestational-age (<10th perc.)	6089	598	Reference	**0.78 (0.65, 0.93)**	0.98 (0.79, 1.22)
			DIFFERENCE BETWEEN TYPES OF EMPLOYMENT STATUS (95% CI)		
Birth weight (grams)	6093		Reference	**84 (53, 114)**	3 (-28, 35)

[#] Adjusted for pregnant women's age, parity, educational level, family income, ethnicity, marital status, psychopathological symptoms, smoking and drinking during pregnancy, BMI, and offspring's gender.
The analyses for birth weight were additionally adjusted for gestational age at birth.
[¶] Compared to spontaneous vaginal delivery.

TABLE 4 presents the adjusted associations between number of weekly working hours and pregnancy outcomes among the employed women. Of all employed participants, 26% (n=1136) worked 1 to 24 h/week, 50% (n=2216) reported to work 25 to 39 h/week, and 26% (n=1056) reported to work ≥40 h/week. Adjusted for confounders, weekly working hours remained significantly associated with birth weight: as the amount of weekly working hours increased, mean birth weight decreased (p for trend=0.044). Compared with children born to women who worked 1 to 24 h/week during pregnancy, working ≥40 h/week was associated with a reduction in mean birth weight of 45 g (95% CI: -89, -1) in the offspring.

TABLE 3A. RISK OF ADVERSE PREGNANCY OUTCOMES AMONG TYPES OF UNEMPLOYMENT AS COMPARED TO PAID EMPLOYMENT[#]

PREGNANCY OUTCOMES	N	OR FOR ADVERSE PREGNANCY OUTCOME (95% CI)				
		EMPLOYED (N=4408)	HOUSEWIFE (N=859)	JOB-SEEKING (N=517)	RECEIVING DISABILITY BENEFIT (N=126)	STUDENT (N=201)
Pregnancy-induced hypertension	5994	Reference	1.31 (0.81, 2.11)	1.12 (0.64, 1.99)	2.22 (1.00, 4.91)	1.81 (0.81, 4.05)
Pre-eclampsia	5994	Reference	0.55 (0.26, 1.16)	1.74 (0.97, 3.15)	0.61 (0.14, 2.65)	1.67 (0.70, 3.98)
Gestational diabetes	5898	Reference	0.53 (0.24, 1.15)	0.61 (0.21, 1.82)	0.93 (0.21, 4.24)	--
Preterm ruptured membranes	5891	Reference	1.03 (0.65, 1.64)	1.54 (0.98, 2.44)	2.62 (1.35, 5.05)	0.70 (0.29, 1.67)
Poor progress of delivery	5888	Reference	1.01 (0.77, 1.32)	0.98 (0.73, 1.32)	0.71 (0.39, 1.28)	0.79 (0.51, 1.24)
Mode of delivery	5585					
Assisted vaginal delivery[¶]		Reference	0.78 (0.58, 1.05)	0.74 (0.53, 1.03)	1.21 (0.71, 2.07)	0.88 (0.56, 1.40)
Elective caesarean delivery[¶]		Reference	0.68 (0.42, 1.11)	0.79 (0.45, 1.37)	1.63 (0.77, 3.45)	1.33 (0.58, 3.02)
Emergency caesarean delivery[¶]		Reference	1.18 (0.82, 1.70)	1.18 (0.80, 1.74)	1.36 (0.69, 2.71)	1.14 (0.60, 2.14)
Preterm birth (<37 weeks)	6110	Reference	0.98 (0.65, 1.47)	1.44 (0.96, 2.16)	**2.35 (1.28, 4.31)**	1.17 (0.61, 2.23)
Meconium-stained amniotic fluid	5833	Reference	1.01 (0.80, 1.29)	1.33 (1.02, 1.74)	1.26 (0.78, 2.02)	1.23 (0.82, 1.85)
Apgar score at 5 minutes (<7)	5907	Reference	1.36 (0.58, 3.20)	1.09 (0.39, 3.02)	**4.19 (1.48, 11.9)**	**3.71 (1.36, 10.1)**
Small-for-gestational-age (<10th perc.)	6089	Reference	1.01 (0.76, 1.34)	1.07 (0.79, 1.45)	0.76 (0.40, 1.44)	1.07 (0.69, 1.68)
		DIFFERENCE BETWEEN TYPES OF UNEMPLOYMENT (95% CI)				
Birth weight (grams)	6093	Reference	24 (-16, 63)	-13 (-61, 35)	-77 (-163, 9)	-49 (-120, 23)

[#] Adjusted for pregnant women's age, parity, educational level, family income, ethnicity, marital status, psychopathological symptoms, smoking and drinking during pregnancy, BMI, and offspring's gender. The analyses for birth weight were additionally adjusted for gestational age at birth.
[¶] Compared to spontaneous vaginal delivery.

TABLE 3B. ASSOCIATION BETWEEN TYPE OF UNEMPLOYMENT AND PREGNANCY OUTCOMES IN SUBGROUP OF UNEMPLOYED PREGNANT WOMEN[#]

PREGNANCY OUTCOMES	N	OR FOR ADVERSE PREGNANCY OUTCOME (95% CI)			
		HOUSEWIFE (N=859)	JOB-SEEKING (N=517)	RECEIVING DISABILITY BENEFIT (N=126)	STUDENT (N=201)
Pregnancy-induced hypertension	1667	Reference	0.95 (0.47, 1.93)	1.69 (0.68, 4.17)	1.54 (0.61, 3.85)
Pre-eclampsia	1667	Reference	2.54 (1.03, 6.26)	1.27 (0.25, 6.34)	2.38 (0.78, 7.27)
Gestational diabetes	1635	Reference	1.10 (0.28, 4.32)	2.39 (0.46, 12.3)	--
Preterm ruptured membranes	1636	Reference	1.73 (0.96, 3.13)	3.16 (1.49, 6.70)	0.76 (0.29, 1.99)
Poor progress of delivery	1635	Reference	0.99 (0.67, 1.45)	0.72 (0.38, 1.36)	0.89 (0.53, 1.48)
Mode of delivery	1543				
Assisted vaginal delivery[¶]		Reference	0.98 (0.63, 1.53)	1.53 (0.84, 2.81)	1.30 (0.75, 2.23)
Elective caesarean delivery[¶]		Reference	1.14 (0.54, 2.40)	2.98 (1.21, 7.34)	1.73 (0.65, 4.62)
Emergency caesarean delivery[¶]		Reference	1.15 (0.69, 1.90)	1.28 (0.60, 2.72)	0.99 (0.48, 2.02)
Preterm birth (<37 weeks)	1702	Reference	1.54 (0.91, 2.62)	2.64 (1.32, 5.28)	1.16 (0.55, 2.45)
Meconium-stained amniotic fluid	1619	Reference	1.25 (0.89, 1.75)	1.23 (0.73, 2.05)	1.08 (0.68, 1.72)
Apgar score at 5 minutes (<7)	1638	Reference	0.61 (0.17, 2.18)	2.84 (0.79, 10.2)	2.47 (0.73, 8.45)
Small-for-gestational-age (<10th perc.)	1701	Reference	1.08 (0.73, 1.60)	0.75 (0.38, 1.49)	1.19 (0.71, 2.01)
		DIFFERENCE BETWEEN TYPES OF UNEMPLOYMENT (95% CI)			
Birth weight (grams)	1688	Reference	-35 (-94, 24)	-97 (-190, -5)	-93 (-174, -12)

[#] Adjusted for pregnant women's age, parity, educational level, family income, ethnicity, marital status, psychopathological symptoms, smoking and drinking during pregnancy, BMI, and offspring's gender. The analyses for birth weight were additionally adjusted for gestational age at birth.
[¶] Compared to spontaneous vaginal delivery.

TABLE 4. ASSOCIATION BETWEEN WEEKLY WORKING HOURS AND PREGNANCY OUTCOMES IN SUBGROUP OF PREGNANT WOMEN WITH PAID EMPLOYMENT[#]

		OR FOR ADVERSE PREGNANCY OUTCOME (95% CI)			
PREGNANCY OUTCOMES	**N**	**1–24 (N=1136)**	**25–39 (N=2216)**	**40 OR MORE (N=1056)**	**P FOR TREND**
Pregnancy-induced hypertension	4327	Reference	0.86 (0.57, 1.30)	0.76 (0.47, 1.24)	0.875
Pre-eclampsia	4327	Reference	0.90 (0.51, 1.61)	0.96 (0.50, 1.84)	0.938
Gestational diabetes	4263	Reference	1.59 (0.78, 3.25)	1.74 (0.69, 4.38)	0.210
Preterm ruptured membranes	4255	Reference	1.19 (0.74, 1.91)	1.35 (0.79, 2.31)	0.278
Poor progress of delivery	4253	Reference	0.89 (0.71, 1.12)	0.83 (0.64, 1.08)	0.174
Mode of delivery	4042				
Assisted vaginal delivery[¶]		Reference	0.98 (0.77, 1.25)	0.98 (0.75, 1.29)	0.916
Elective caesarean delivery[¶]		Reference	1.03 (0.70, 1.50)	1.06 (0.68, 1.66)	0.796
Emergency caesarean delivery[¶]		Reference	0.95 (0.69, 1.31)	0.76 (0.52, 1.11)	0.126
Preterm birth (<37 weeks)	4408	Reference	1.37 (0.91, 2.06)	1.30 (0.81, 2.10)	0.345
Meconium-stained amniotic fluid (yes)	4214	Reference	1.00 (0.80, 1.25)	1.12 (0.86, 1.46)	0.399
Apgar score at 5 minutes (<7)	4269	Reference	0.62 (0.27, 1.41)	0.94 (0.38, 2.35)	0.982
Small-for-gestational-age (<10th perc.)	4403	Reference	0.95 (0.72, 1.25)	1.01 (0.73, 1.39)	0.924
		DIFFERENCE BETWEEN TYPES OF UNEMPLOYMENT (95% CI)			
Birth weight (grams)	4405	Reference	-21 (-56, 15)	**-45 (-89, -1)**	0.044

[#] Adjusted for pregnant women's age, parity, educational level, family income, ethnicity, marital status, psychopathological symptoms, smoking and drinking during pregnancy, BMI, and offspring's gender. The analyses for birth weight were additionally adjusted for gestational age at birth.
[¶] Compared to spontaneous vaginal delivery.

DISCUSSION

The results of this large birth cohort study showed that, after correction for confounders, employed and unemployed women have the same risk of pregnancy complications. Though, within the subgroups of unemployed and employed women, we observed differences in pregnancy outcomes. Among unemployed pregnant women, those who receive disability benefit seem to be at highest risk of pregnancy complications. In the subgroup of women with paid employment, long weekly working hours during pregnancy were associated with a lower birth weight in the offspring.

EMPLOYMENT STATUS AND PREGNANCY COMPLICATIONS

Regarding the association between employment status and pregnancy complications, a mixed pattern was observed. On the one hand, our study indicated that paid employment among pregnant women, as compared to unemployment, was associated with a lower risk of several pregnancy complications, i.e. preterm ruptured membranes, preterm birth, meconium-stained amniotic fluid and SGA. Moreover, employment was associated with a higher mean birth weight than unemployment. These observations are along the lines of the 'healthy worker effect' that implies better health outcomes among employed persons.[5] Nevertheless, caution is needed when interpreting the 'healthy worker effect', as it is frequently the consequence of confounding factors.[23 24] Indeed, after adjustment for confounders, being employed was no longer associated with better pregnancy outcomes than being unemployed: the lower risks for pregnancy complications among employed women were entirely explained by epiphenomena of employment status, specifically the combination of more optimal socio-economic circumstances (i.e. higher education and income) and better mental health of these women.

On the other hand, employed pregnant women also had an *increased* risk of adverse outcomes that mainly involved complications at delivery, such as poor progress of delivery and non-spontaneous delivery. These associations were entirely attributable to parity. The explanation for this is that the employed women in our study were more often nulliparous than unemployed women, and that giving birth for the first time is associated with a relatively high risk of such obstetric complications.[25]

Defining statistical significance at a p-value below 0.05, we found that employment status was not associated with pregnancy complications. However, some of the relations just missed this level of statistical significance. This concerned the decreased risk of pregnancy-induced hypertension and non-optimal Apgar score as well as the increased risk of gestational diabetes and assisted vaginal delivery among employed women as compared to unemployed women. It might be that these associations did not reach statistical significance due to a small number of cases. Therefore, it is important that our findings are replicated in large population based studies with a sufficient number of cases of these pregnancy complications. In the unemployed group, women receiving disability benefit had the highest

risk of several pregnancy complications. The findings on mode of delivery indicate that obstetricians often decide in advance to end pregnancies of women receiving disability benefit with an elective caesarean section. This may be done to reduce health risks for both mother and child. Hypothetically, ill health of women receiving disability benefit is the cause of both their unemployment and their increased risk of complicated pregnancies. Unfortunately, we were unable to control for pre-existing physical health status of the pregnant women, as we lacked information on this topic. We also showed that the mean birth weight of offspring of women receiving disability benefit and of students was lower as compared to offspring of housewives. The explanation for this might be differences in levels of stress or variations in dietary and exercise patterns, which are known to be related to birth weight in the offspring.[26 27 28 3] Finally, the analyses among unemployed women indicated that offspring of students and of women receiving disability benefit had an increased risk of a non-optimal Apgar score after birth as compared to employed women. Further research is necessary to replicate this result, as this has, to our knowledge, not been reported before and because the analyses were performed on small groups.

Among employed women, we observed that long weekly working hours during pregnancy were associated with a lower birth weight in the offspring. This is in contrast to earlier studies that reported no association.[8 9 12 13] These studies, however, examined birth weight in a dichotomized way, while we analyzed birth weight continuously whereby differences are detected more rapidly. Besides methodological considerations, such as multiple testing and residual confounding, there may be other reasons for the observed inverse association between working hours and birth weight. Women who work full-time might experience more stress than those working part-time. Stress during pregnancy is known to be associated with reduced blood flow through the uterine arteries.[29] This may, in turn, affect foetal development and thus birth weight. Alternatively, the lower birth weight among women with long weekly working hours might also be explained by more frequent exposure to work related hazards, such as prolonged standing[12] or pesticides[30].

METHODOLOGICAL CONSIDERATIONS

Several methodological considerations need to be addressed. The participants of the Generation R cohort represent a selection towards a relatively healthy population.[31 32] Moreover, the non-response analyses indicated that data were more complete in higher educated, non-single, older, and non-smoking pregnant women of Dutch origin. Women with missing data on employment had a higher risk of some, but not all pregnancy complications as compared to women without missing data. So, the selective participation and response resulted in an underrepresentation of pregnant women of the most disadvantaged groups, who are at increased risk for pregnancy complications. This might restrict the external validity of our study, especially if the relation between employment characteristics and pregnancy complications differed between participating and non-participating women. Despite our large study population, another limitation is the low prevalence rates of some

of the pregnancy complications. For instance, only 66 women had gestational diabetes and only 63 babies had an Apgar score <7 at 5 minutes after birth; consequently, there was limited power to detect significant differences. Moreover, while the diagnostic criteria used to identify cases of gestational diabetes in the present study compare well with those used by the American Diabetes Association[33] some cases of gestational diabetes may have been missed, as suggested by our relatively low incidence of gestational diabetes.[34] This is probable because measurement of blood glucose levels was not a standard prenatal procedure, whereby cases of gestational diabetes without overt symptoms might have remained unrecognized by the prenatal caregiver. Another shortcoming is that assessment of employment characteristics occurred at only one time point during pregnancy; however, we assume that these conditions generally remain relatively stable until maternity leave. Furthermore, the use of self-reports of alcohol consumption and smoking during pregnancy is also a limitation, as this may result in reporter bias. Finally, the adjustment for some confounding factors may have resulted in over-adjustment of the analyses.

This pertains particularly to family income, as it is plausible that unemployment leads to pregnancy complications via restricted financial resources and worries about financial issues. Nevertheless, exclusion of family income from the adjusted analyses on the effect of employment status on pregnancy complications did not result in different findings and conclusions. The covariates educational level, parity and psychopathological symptoms may be, at least in part, preceding factors in the association between paid employment and pregnancy complications. However, as it is not probable that the effect of these covariates on pregnancy complications is completely mediated by employment status, these covariates should be considered as confounding factors rather than as antecedents.

IMPLICATIONS AND CONCLUSIONS

Because our study is one of the first to examine the relation between employment status and weekly working hours with a wide range of pregnancy complications, more research is needed to replicate and complement our findings. It is important to elucidate the underlying mechanisms for our findings that women receiving disability benefit have an increased risk of pregnancy complications and that different types of unemployment and long weekly working hours are associated with a lower birth weight. Because commencement of maternity leave may be intertwined with the effect of weekly working hours on birth weight, future studies should also take this factor into consideration.

In conclusion, we found no indications that paid employment during pregnancy benefits or endangers the health of mother and child. The subgroups of employed and unemployed women proved, nevertheless, to be relatively heterogeneous: women receiving disability benefit had an elevated risk of preterm delivery than housewives. Moreover, offspring of students, of women receiving disability benefit and of women with long working hours during pregnancy had a lower mean birth

weight. More research is needed to confirm these findings and to provide explanations for these results. In the meanwhile, prenatal care providers should be made aware of the risk of pregnancy complications among women receiving disability benefit and students, and of the offspring's lower mean birth weight among women receiving disability benefit, students and women with long working hours during pregnancy. Perhaps extensive monitoring and counselling by prenatal care providers leads to a reduction in the risks of pregnancy complications among these women. Future research should examine whether this is an effective strategy.

REFERENCES

1. Statistical Office of the European Communities. http://epp.eurostat.ec.europa.eu 2008.
2. Jin RL, Shah CP, Svoboda TJ. The impact of unemployment on health: a review of the evidence. *Cmaj* 1995;153(5):529-40.
3. Mathers CD, Schofield DJ. The health consequences of unemployment: the evidence. *Med J Aust* 1998;168(4):178-82.
4. Weich S, Lewis G. Poverty, unemployment, and common mental disorders: population based cohort study. *Bmj* 1998;317(7151):115-9.
5. Schuring M, Burdorf L, Kunst A, Mackenbach J. The effects of ill health on entering and maintaining paid employment: evidence in European countries. *J Epidemiol Community Health* 2007;61(7):597-604.
6. Nguyen N, Savitz DA, Thorp JM. Risk factors for preterm birth in Vietnam. *Int J Gynaecol Obstet* 2004;86(1):70-8.
7. Hanke W, Saurel-Cubizolles MJ, Sobala W, Kalinka J. Employment status of pregnant women in central Poland and the risk of preterm delivery and small-for-gestational-age infants. *Eur J Public Health* 2001;11(1):23-8.
8. Savitz DA, Olshan AF, Gallagher K. Maternal occupation and pregnancy outcome. *Epidemiology* 1996;7(3):269-74.
9. Gabbe SG, Turner LP. Reproductive hazards of the American lifestyle: work during pregnancy. *Am J Obstet Gynecol* 1997;176(4):826-32.
10. Saurel-Cubizolles MJ, Zeitlin J, Lelong N, Papiernik E, Di Renzo GC, Breart G, et al. Employment, working conditions, and preterm birth: results from the Europop case-control survey. *J Epidemiol Community Health* 2004;58(5):395-401.
11. Rodrigues T, Barros H. Maternal unemployment: an indicator of spontaneous preterm delivery risk. *Eur J Epidemiol* 2008;23(10):689-93.
12. Croteau A, Marcoux S, Brisson C. Work activity in pregnancy, preventive measures, and the risk of delivering a small-for-gestational-age infant. *Am J Public Health* 2006;96(5):846-55.
13. Bonzini M, Coggon D, Palmer KT. Risk of prematurity, low birthweight and pre-eclampsia in relation to working hours and physical activities: a systematic review. *Occup Environ Med.* 2007;64(4):228-43.
14. Mozurkewich EL, Luke B, Avni M, Wolf FM. Working conditions and adverse pregnancy outcome: a meta-analysis. *Obstet Gynecol* 2000;95(4):623-35.
15. Saftlas AF, Logsden-Sackett N, Wang W, Woolson R, Bracken MB. Work, leisure-time physical activity, and risk of preeclampsia and gestational hypertension. *Am J Epidemiol* 2004;160(8):758-65.
16. Hung S, Morrison DR, Whittington LA, Fein SB. Prepartum work, job characteristics, and risk of cesarean delivery. *Birth* 2002;29(1):10-7.
17. Jaddoe VW, Bakker R, van Duijn CM, van der Heijden AJ, Lindemans J, Mackenbach JP, et al. The Generation R Study Biobank: a resource for epidemiological studies in children and their parents. *Eur J Epidemiol* 2007;22(12):917-23.
18. Jaddoe VW, van Duijn CM, van der Heijden AJ, Mackenbach JP, Moll HA, Steegers EA, et al. The Generation R Study: design and cohort update until the age of 4 years. *Eur J Epidemiol* 2008.
19. Brown MA, Lindheimer MD, de Swiet M, Van Assche A, Moutquin JM. The classification and diagnosis of the hypertensive disorders of pregnancy: statement from the International Society for the Study of Hypertension in Pregnancy (ISSHP). *Hypertens Pregnancy* 2001;20(1):IX-XIV.

20. Verburg BO, Steegers EA, De Ridder M, Snijders RJ, Smith E, Hofman A, et al. New charts for ultrasound dating of pregnancy and assessment of fetal growth: longitudinal data from a population-based cohort study. *Ultrasound Obstet Gynecol* 2008;31(4):388-96.
21. Kramer MS, Platt RW, Wen SW, Joseph KS, Allen A, Abrahamowicz M, et al. A new and improved population-based Canadian reference for birth weight for gestational age. *Pediatrics* 2001;108(2):E35.
22. Derogatis LR. *Brief Symptom Inventory (BSI): Administration, scoring and procedures. Manual, third edition*. Minneapolis, MN, USA, 1993.
23. Pearce N, Checkoway H, Kriebel D. Bias in occupational epidemiology studies. *Occup Environ Med* 2007;64(8):562-8.
24. Li CY, Sung FC. A review of the healthy worker effect in occupational epidemiology. *Occup Med (Lond)* 1999;49(4):225-9.
25. Bai J, Wong FW, Bauman A, Mohsin M. Parity and pregnancy outcomes. *Am J Obstet Gynecol* 2002;186(2):274-8.
26. Valero De Bernabe J, Soriano T, Albaladejo R, Juarranz M, Calle ME, Martinez D, et al. Risk factors for low birth weight: a review. *Eur J Obstet Gynecol Reprod Biol.* 2004;116(1):3-15.
27. Mulder EJ, Robles de Medina PG, Huizink AC, Van den Bergh BR, Buitelaar JK, Visser GH. Prenatal maternal stress: effects on pregnancy and the (unborn) child. *Early Hum Dev.* 2002;70(1-2):3-14.
28. Hobel C, Culhane J. Role of psychosocial and nutritional stress on poor pregnancy outcome. *J Nutr.* 2003;133(5 Suppl 2):1709S-1717S.
29. Teixeira JM, Fisk NM, Glover V. Association between maternal anxiety in pregnancy and increased uterine artery resistance index: cohort based study. *Bmj* 1999;318(7177):153-7.
30. Burdorf A, Brand T, Jaddoe VWV, Hofman A, Mackenbach JP, Steegers EAP. The effects of work-related maternal risk factors on time to pregnancy, preterm birth and birth weight. The Generation R Study. . *Under review: Occupational and Environmental Medicine.*
31. Center for Research and Statistics, Rotterdam (COS). http://www.cos.rotterdam.nl. 2005.
32. Jaddoe VW, Mackenbach JP, Moll HA, Steegers EA, Tiemeier H, Verhulst FC, et al. The Generation R Study: Design and cohort profile. *Eur J Epidemiol.* 2006;21(6):475-84.
33. American Diabetes Association. Gestational diabetes mellitus. *Diabetes Care* 2004;27 Suppl 1:S88-90.
34. van Leeuwen M, Zweers EJ, Opmeer BC, van Ballegooie E, ter Brugge HG, de Valk HW, et al. Comparison of accuracy measures of two screening tests for gestational diabetes mellitus. *Diabetes Care* 2007;30(11):2779-84.

CHAPTER 3

SOCIAL DISADVANTAGE AND EARLY CHILDHOOD BEHAVIOUR

CHAPTER **3.1**

Socioeconomic inequalities in infant temperament

ABSTRACT

BACKGROUND: A low socioeconomic status (SES) has consistently been associated with behavioural problems during childhood. The studies of SES and behaviour in infants used temperament as a behavioural measure. However, these studies in younger children yielded inconsistent findings. Furthermore, they generally did not examine explanatory mechanisms underlying the association between SES and temperament. We investigated the association between SES and temperament in infancy.

METHODS: The study was embedded in the Generation R study, a population-based cohort in The Netherlands. Maternal and paternal education, family income, and maternal occupational status were used as indicators of SES. At the age of six months, 4055 mothers filled out six scales of the Infant Behaviour Questionnaire-Revised.

RESULTS: Lower SES was associated with more difficult infant temperament as measured by five of the six temperament dimensions (e.g. Fear: unadjusted z-score difference between lowest and highest education: 0.57 (95%CI: 0.43, 0.71)). Only the direction of the association between SES and Sadness was reversed. The effect of SES on Distress to Limitations, Recovery from Distress, and Duration of Orienting scores was largely explained by family stress and maternal psychological well-being. These covariates could not explain the higher levels of Activity and Fear nor the lower Sadness scores of infants from low SES groups.

CONCLUSIONS: SES inequalities in temperament were already present in six months old infants and could partially be explained by family stress and maternal psychological well-being. The results imply that socioeconomic inequalities in mental health in adults may have their origin early in life.

INTRODUCTION

Socioeconomic inequalities in mental health during childhood are well documented. Research within different age ranges has indicated that children from families with a low socioeconomic status (SES) exhibit higher rates of overall problem behaviour as measured by behaviour checklists than children from higher SES families.[1-6] Similarly, clinically diagnosed psychopathology is more prevalent among children from lower SES families, although the strength of this association varies by type of psychiatric disorder.[7 8] The effects of SES were particularly consistent for disruptive behaviour disorders[8 9], ADHD[10], and depression[9 11], while an association between SES and, for example, pervasive developmental disorders is not evident[12]. The mechanisms through which SES influences children's psychosocial well-being are not completely understood; however, some mediating factors have been identified. Research has indicated that a young maternal age and single parenthood explain part of the association.[7 13]

The above mentioned studies were conducted in school-aged children. Research regarding socioeconomic inequalities in mental health of infants used temperament as a behavioural measure, which is one possible way to conceptualize early emotional differences. Temperamental traits are relatively stable across the lifespan[14 15] and are shaped by both genetic and environmental factors[16 17]. There are methodological difficulties when relating temperament dimensions to children's risk for psychopathology.[18 19] However, several studies argued that temperamental difficulties predict later behavioural problems.[16 17 20] For instance, Schwartz et al.[21] reported that an inhibited temperament (subdued to and avoidant of novelty) in the second year of life predisposes children to social anxiety in adolescence. A difficult temperament in infancy is also associated with other adverse outcomes in childhood and adolescence (e.g. poor school achievement[22], language impairment[23], and problems with peers[24]). Little research on the association between SES and infant temperament has been carried out. Most of these studies found no or minimal evidence of a socioeconomic gradient in infant temperament;[25-27] only Sameroff et al.[28] reported that infants of lower SES families had a more difficult temperament. Because of these contradictory findings, it has remained unclear whether socioeconomic differences in temperament are already present in infancy.

Little attention has been paid to the explanatory mechanisms behind the association between SES and temperament. Probably, these mechanisms are at least partly similar to explanatory pathways through which SES influences behaviour of school-aged children, i.e. maternal age and single parenthood.[3 7] However, other risk factors of behavioural problems may also be involved. In a review, Campbell[29] concluded that many indicators of maternal psychological well-being and family stress are associated with problem behaviour in preschool children. Examples of these indicators are symptoms of maternal psychopathology and general malaise, marital dissatisfaction, and stressful life events in the past year. In the same review birth weight was listed as a biological risk factor of later behavioural problems.[29] Furthermore, many other review studies indicated maternal smoking during preg-

nancy as a risk factor for child behavioural problems.[30 31] As these risk factors of behavioural problems are associated with SES, they possibly explain the relation between SES and temperament.

The aim of the present study was to examine the association between socioeconomic status and temperament in infants six months of age. We analyzed the different indicators of SES, namely maternal and paternal education, maternal occupational status, and family income, separately, in order to study the differential effects of the SES components and obtain results easy to interpret.[32] Furthermore, we explored the following possible explanatory mechanisms underlying this relation: sociodemographic characteristics (maternal age and marital status), family stress (long lasting difficulties and family functioning), and maternal psychological well-being (psychopathology, self-esteem and confidence in caretaking). We hypothesized that (i) a lower socioeconomic status is associated with less favourable temperament scores of the infants and (ii) this effect is largely explained by sociodemographic characteristics, family stress, and maternal psychological well-being.

METHODS

DESIGN

This study was embedded in the Generation R Study, a population-based cohort study from fetal life until young adulthood.[33] Briefly, pregnant women living in the study area in Rotterdam, The Netherlands, with an expected delivery date between April 2002 and January 2006, were invited to participate. Written informed consent was obtained from all participants. The Medical Ethical Committee of the Erasmus Medical Center, Rotterdam, has approved the study.

POPULATION FOR ANALYSIS

Full consent for the postnatal phase of the Generation R Study was obtained from 7295 infants and their mothers. Those without information on maternal education (n=662) were excluded from the present study. Infants with missing data on temperament at six months, either due to logistic problems at our research center (n=1161) or because of non-response (n=1417), were also excluded, yielding a sample size of 4055 infants for the present analyses. The response rate for the temperament questionnaire was 74% (4055 / 5472). Due to missing data, the study population varies per indicator of SES. The study population consisted of 2001 boys and 2054 girls with a mean age of 6.7 months. The ethnic breakdown of the sample was: 2631 Dutch children, 395 Other Western children, and 1027 children of non-Western background.

SOCIOECONOMIC STATUS

Information on different indicators of SES was obtained by questionnaire during pregnancy. Maternal and paternal education were defined as the highest attained educational level and divided into five categories ranging from primary education

only (I) to university (V) [34]. Family income, defined by the total net monthly income of the household, was categorized as '<1200 euros', '1200-2000 euros', and '>2000 euros'. Maternal occupational status was coded from I (low occupation) to V (high occupation) following the method of the Dutch Central Bureau of Statistics.[35]

INFANT TEMPERAMENT

At the age of six months, infant temperament was assessed using an adapted version of the Infant Behaviour Questionnaire-Revised (IBQ-R).[36] A detailed description of the changes has previously been described.[37] Briefly, we assessed six scales of the IBQ-R: Activity Level (e.g. movements of arms and legs); Distress to Limitations (e.g. fussing or crying while in caretaking activities); Duration of Orienting (e.g. attention to a single object for extended periods of time); Sadness (e.g. general low mood); Fear (e.g. startle or distress to novelty or sudden changes in stimulation); and Recovery from Distress (e.g. rate of recovery from general arousal; ease of falling asleep). Higher scores on the scales, except for Recovery from Distress, indicate a more difficult temperament. The 74 assessed items ask mothers to rate the frequency of certain behaviours in specified contexts across the previous week on a three-point scale (0=never present, 1=sometimes present, 2=often present). The total score of a scale was defined as missing, if more than 25% of the items in a scale were not filled out. Internal consistencies for the adapted IBQ-R ranged from α=0.70 (Duration of Orienting) to α=0.85 (Fear), which is satisfactory and comparable to the internal consistencies of the original IBQ-R.[36]

COVARIATES

On conceptual grounds, a distinction was made between confounders and mediators, two statistically identical concepts. The mediation hypothesis states that there is a causal relation between an independent, a third and dependent variable, while confounding does not necessarily imply a causal relationship between a third and other variables.[38] Infant gender, age and ethnicity were considered as confounders, since they can bias the association, but are not on the causal pathway between socioeconomic status and infant temperament, in contrast to the other covariates under study.

Sociodemographic characteristics, family stress, maternal psychological well-being, maternal smoking during pregnancy and infant birth weight were studied as potential mediators. Information on the sociodemographic characteristics maternal age and marital status ('Married or cohabiting' and 'Single parenthood') was obtained by questionnaire. Family stress was assessed by questionnaire with the Long Lasting Difficulties checklist[39] and the General Functioning Scale of the Family Assessment Device[40]. Maternal psychological well-being included maternal psychopathology during pregnancy and again two months postpartum using the Brief Symptom Inventory, a validated self-report questionnaire which consists of positive and negative self-appraisal statements.[41] We evaluated global self-esteem with the Rosenberg Self-Esteem Scale.[42] The final measure of psychological well-being was the subscale Lack of Confidence in Caretaking of the Mother and Baby

Scales.[43] Two months after birth of their child, the mothers filled out this scale, with lower scores denoting more confidence in looking after the baby.

STATISTICAL ANALYSES

The infants' temperament scores were z-standardized in the current study. The standardized differences between the mean temperament scores of different SES groups can thus be evaluated according to Cohen's criteria.[44] The Fear scores had a right skewed distribution and were therefore log transformed. Linear regression was used to examine the association between SES and the six temperament scales. We conducted these analyses for each indicator of SES separately. The values presented in TABLES 2, 3 and 4 reflect differences in IBQ-R scores between the highest SES group (reference group) and the other SES groups. The confounders infant age and ethnicity were included in the primary analyses. As gender did not meaningfully change the effect estimates, this covariate was not included as confounder. All fully adjusted associations were controlled for sociodemographic characteristics, family stress, as well as maternal psychological well-being. Adjustment for birth weight and smoking habits did not meaningfully change the effect estimates. Therefore, these covariates were not included in the adjusted analyses. Stepwise adjustment is presented for two IBQ-R scales to illustrate the influence of specific covariates. We chose this statistical approach of regression adjustment and did not apply formal mediation criteria, as variables may be explanatory in the absence of significant associations with both the determinant and outcome.[38] Multiple imputation (function AregImpute in Splus 6.0) was applied to substitute missing data of the covariates, by using the relations between the variables in the dataset.[45] Because the substitution procedure was repeated five times, multiple imputation took into account the uncertainty of the imputed values. All statistical analyses were performed using Statistical Package of Social Sciences version 11.0 for Windows (SPSS Inc, Chicago, IL, USA) and Splus 6.0 Professional Release 1.

NON-RESPONSE ANALYSES

Mothers with missing data on infant temperament (n=2578), either due to logistic problems or because of non-response, were compared with mothers who filled out the IBQ-R (n=4055). Data on temperament was more often missing (n=2578) in mothers who were lower educated (χ^2=259; df=4; p<0.001), non-Western (χ^2=134; df=2; p<0.001), single parent (χ^2=89; df=1; p<0.001), and younger (F-test=114; df=1; p<0.001) as compared to mothers who filled out the temperament questionnaire.

RESULTS

Characteristics of the mothers and infants per educational category are presented in TABLE 1. The lowest educated mothers were younger as compared to mothers with the highest education (F-test=159; df=4; p<0.001). They were also more often single (χ^2=128; df=1; p<0.001), experienced higher levels of family stress (F-test=58; df=4; p<0.001), and reported more Long Lasting Difficulties (F-test=31; df=4; p<0.001) and psychopathological symptoms (prenatal: F-test=60; df=4; p<0.001; postpartum: F-test=28; df=4; p<0.001). Moreover, the infants of the lowest educated mothers were more often non-Dutch (82.3%) than infants of the highest educated mothers (23.5%; χ^2=276; df=1; p<0.001).

TABLE 1. CHARACTERISTICS OF MOTHERS AND THEIR INFANTS ACCORDING TO LEVEL OF MATERNAL EDUCATION

	LEVEL OF MATERNAL EDUCATION (N=4055)				
	V (HIGHEST) (N=1290)	IV (N=970)	III (N=1146)	II (N=406)	I (LOWEST) (N=243)
Sociodemographic characteristics					
Age (years)	33.2 ± 3.2	31.8 ± 4.0 ***	29.9 ± 4.9 ***	28.3 ± 5.6 ***	28.4 ± 5.9 ***
Marital status (% single)	2.7	5.5 **	12.7 ***	20.5 ***	22.3 ***
Family stress					
Long Lasting Difficulties (score)	1.6 ± 2.3	2.1 ± 2.7 **	3.0 ± 3.7 ***	3.0 ± 3.5 ***	3.5 ± 4.2 ***
Family Assessment Device (score)	1.4 ± 0.4	1.5 ± 0.4 **	1.6 ± 0.5 ***	1.7 ± 0.5 ***	1.8 ± 0.5 ***
Maternal psychological well-being					
Prenatal psychopathology (score)	0.16 ± 0.2	0.20 ± 0.2 **	0.29 ± 0.4 ***	0.37 ± 0.4 ***	0.45 ± 0.5 ***
Postpartum psychopathology (score)	0.16 ± 0.2	0.21 ± 0.3 **	0.27 ± 0.4 ***	0.28 ± 0.4 ***	0.38 ± 0.5 ***
Rosenberg Self-Esteem Scale (score)	4.5 ± 0.5	4.4 ± 0.5 *	4.3 ± 0.6 ***	4.2 ± 0.6 ***	4.0 ± 0.7 ***
Lack of Confidence in Caretaking (score)	14.3 ± 10.4	13.9 ± 10.1	13.5 ± 10.2	11.8 ± 10.5 ***	12.5 ± 9.3 *
Other covariates					
Smoking during pregnancy					
No (%)	87.9	81.5 ***	73.6 ***	57.0 ***	67.6 ***
Until pregnancy was known (%)	7.8	9.9	9.5	9.1	6.7
Continued during pregnancy (%)	4.3	9.9 ***	16.9 ***	33.9 ***	25.7 ***
Birth weight (grams)	3504 ± 559	3460 ± 545	3394 ± 575 ***	3367 ± 567 ***	3350 ± 541 ***
Confounders					
Gender (% boys)	48.5	49.4	50.3	49.3	49.0
Infant age (months)	6.6 ± 1.2	6.7 ± 1.4	6.7 ± 1.1	6.6 ± 1.2	6.8 ± 1.5 *
Infant ethnicity					
Dutch (%)	76.5	72.2 *	59.4 ***	54.4 ***	17.7 ***
Other Western (%)	12.2	10.7	8.3 **	5.4 ***	7.0 *
Non-Western (%)	11.3	17.0 ***	32.3 ***	40.1 ***	75.3 ***

Values are means ± standard deviation for continuous variables and percentages for categorical variables.
** p-value < 0.05, ** < 0.01, *** < 0.001;*
ANOVA for continuous variables, χ^2 tests for categorical variables, vs. highest educational level (V).

TABLE 2 shows the association between maternal education and infant temperament scores. Mothers with low education as compared to mothers with high education had infants with a more difficult temperament, characterized by higher scores on Activity Level, Duration of Orienting, and Fear (p for trend <0.001, 0.003 and <0.001, respectively). The overall trend of SES inequalities in Distress to Limitations and Recovery from Distress was statistically non-significant (p for trend =0.30 and =0.07, respectively), although infants of the lowest educated mothers had worse scores than infants of the highest educated mothers on both scales (age and ethnicity adjusted differences: 0.172 (95% CI: 0.029, 0.315; p=0.02) and -0.175 (95% CI: -0.323, -0.026; p=0.02), respectively). These differences in Distress to Limitations and Recovery from Distress scores were no longer statistically significant after adjustment for sociodemographic characteristics, stress, and maternal psychological well-being (adjusted differences: 0.032 (95% CI: -0.113, 0.178; p=0.67) and -0.092 (95% CI: -0.241, 0.057; p=0.23), respectively). Educational differences in Duration of Orienting scores were also substantially reduced by adjusting, and did not reach significance anymore (p for trend =0.13). The differences in Activity Level and Fear scores between infants of the highest and lowest educated mothers decreased only marginally after adjustment for the covariates (adjusted differences: 0.213 (95% CI: 0.068, 0.358; p=0.004) and 0.434 (95% CI: 0.289, 0.579; p<0.001), respectively). Compared to the other temperament dimensions, the direction of the association between education and Sadness was reversed: infants of higher educated mothers had higher Sadness scores than infants of lower educated mothers (p for trend <0.001). The difference in Sadness scores between infants of the highest and lowest educated mothers was even more marked after full adjustment (fully adjusted difference: -0.282 (95% CI: -0.429, -0.135; p<0.001)).

TABLE 3 presents the fully adjusted relation between different indicators of SES with infant temperament scores. Consistent with the results of the analyses with maternal education, both low maternal occupational status and low family income were associated with a more difficult infant temperament as measured with the dimensions Activity Level and Fear (p for trends <0.001). Additionally, infants of families with a low income also had significantly lower scores on the Sadness scale (p for trend <0.001). Maternal occupational status and family income were not related to the other temperamental dimensions. Again consistent with the other SES indicators, infants of low educated fathers had significantly higher scores on Activity Level and Fear as compared to infants of high educated fathers (fully adjusted differences: 0.261 (95% CI: 0.090, 0.432; p=0.003) and 0.273 (95% CI: 0.102, 0.444; p=0.002), respectively). In contrast to above two temperament scales, low paternal education was also associated with lower scores on Distress to Limitations and Sadness (p for trend 0.001 and <0.001, respectively), indicating less temperamental problems. Paternal educational level was not related to Duration of Orienting and Recovery from Distress (p for trend 0.397 and 0.318, respectively).

TABLE 2. LEVEL OF MATERNAL EDUCATION AND INFANT TEMPERAMENT, UNADJUSTED AND FULLY ADJUSTED

LEVEL OF MATERNAL EDUCATION	N[#]	ACTIVITY LEVEL	DISTRESS TO LIMITATIONS	DURATION OF ORIENTING	SADNESS	FEAR[¶]	RECOVERY FROM DISTRESS [§]
		AGE AND ETHNICITY ADJUSTED DIFFERENCES[°]					
V (highest)	1290	0(reference)	0(reference)	0(reference)	0(reference)	0(reference)	0(reference)
IV	970	0.015(0.041)	-0.066(0.041)	0.056(0.043)	-0.032(0.043)	0.122(0.041)**	0.017(0.042)
III	1146	0.217(0.040)***	-0.006(0.040)	0.138(0.042)**	-0.097(0.042)*	0.174(0.040)***	-0.007(0.041)
II	406	0.290(0.056)***	-0.046(0.056)	0.192(0.058)**	-0.278(0.058)***	0.240(0.056)***	-0.049(0.058)
I (lowest)	243	0.380(0.073)***	0.172(0.073)*	0.018(0.076)	-0.155(0.076)	0.570(0.070)***	-0.175(0.076)*
p for trend		‹0.001	0.296	0.003	‹0.001	‹0.001	0.073
		FULLY ADJUSTED DIFFERENCES[†]					
V (highest)	1290	0(reference)	0(reference)	0(reference)	0(reference)	0(reference)	0(reference)
IV	970	-0.033(0.040)	-0.097(0.040)*	0.039(0.043)	-0.053(0.041)	0.093(0.040)*	0.034(0.041)
III	1146	0.100(0.041)*	-0.093(0.041)*	0.098(0.043)*	-0.162(0.042)***	0.095(0.041)*	0.050(0.042)
II	406	0.123(0.058)*	-0.167(0.058)**	0.135(0.062)*	-0.350(0.059)***	0.136(0.058)*	0.018(0.060)
I (lowest)	243	0.213(0.074)**	0.032(0.074)	-0.033(0.078)	-0.282(0.075)***	0.434(0.074)***	-0.092(0.076)
p for trend		‹0.001	0.101	0.129	‹0.001	‹0.001	0.863

Values are regression coefficients and reflect differences in z-scores (standard error) between a certain educational level and the reference group, i.e. highest educational level (V).
[#] Gives number of infants per educational level that were included in the analyses of at least one temperament scale (maximum 10.7% less subjects per educational level).
[¶] Fear was log transformed.
[§] In contrast to all other scales, higher scores on Recovery from Distress indicate less temperamental problems.
** Indicates a significant difference from the reference group, p-value ‹ 0.05, ** p-value ‹ 0.01, *** p-value ‹ 0.001.*
° Adjusted for infant age and infant ethnicity.
† Adjusted for sociodemographic characteristics (maternal age, marital status), family stress (Long Lasting Difficulties, Family Assessment Device) and maternal psychological well-being (prenatal and postpartum psychopathology, Rosenberg Self-Esteem Scale, Lack of Confidence in Caretaking).

To illustrate the explanatory effect of several variables on socioeconomic differences in temperament, stepwise covariate adjustment for two selected temperament dimensions is presented in TABLE 4. The explanatory effect of the covariates on these two dimensions are prototypical. Sociodemographic characteristics accounted for 35% ((0.172 – 0.111) / 0.172) of the difference in Distress to Limitations scores between infants of the highest and lowest educated mothers. In contrast, family stress and maternal psychological well-being explained a larger part of the score differences between infants of the highest and lowest educated mothers, 52% and 53%, respectively. The percentages add up to more than 100% due to overlap between different explanatory variables. The explanatory models of Activity Level scores followed a different pattern: family stress and maternal psychological well-being accounted for only 18% and 22%, respectively, while sociodemographic variables explained 28% of the differences between infants of the highest and lowest educated mothers.

TABLE 3. INDICATORS OF SOCIOECONOMIC STATUS AND INFANT TEMPERAMENT (ALL FULLY ADJUSTED†)

	N#	ACTIVITY LEVEL	DISTRESS TO LIMITATIONS	DURATION OF ORIENTING	SADNESS	FEAR¶	RECOVERY FROM DISTRESS§
LEVEL OF PATERNAL EDUCATION							
V (highest)	1076	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)
IV	626	0.058 (0.048)	-0.106 (0.048) *	0.009 (0.050)	-0.102 (0.049) *	-0.013 (0.048)	-0.016 (0.049)
III	729	0.075 (0.047)	-0.179 (0.048) ***	0.083 (0.050)	-0.178 (0.048) ***	0.044 (0.048)	0.112 (0.048) *
II	329	0.207 (0.062) **	-0.204 (0.063) **	0.026 (0.066)	-0.195 (0.063) **	0.147 (0.063) *	0.130 (0.041) *
I (lowest)	155	0.261 (0.087) **	-0.062 (0.086)	0.016 (0.090)	-0.187 (0.088) *	0.273 (0.087) **	-0.156 (0.088)
p for trend		<0.001	0.001	0.397	<0.001	0.001	0.318
MATERNAL OCCUPATIONAL STATUS							
V (highest)	242	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)
IV	870	-0.004 (0.069)	0.048 (0.070)	-0.018 (0.073)	0.008 (0.070)	0.006 (0.070)	-0.076 (0.070)
III	991	0.021 (0.068)	-0.092 (0.069)	0.042 (0.072)	-0.038 (0.070)	0.090 (0.069)	-0.031 (0.070)
II	838	0.152 (0.071) *	-0.071 (0.072)	0.076 (0.075)	-0.092 (0.073)	0.158 (0.072) *	-0.068 (0.073)
I (lowest)	136	0.406 (0.107) ***	0.148 (0.108)	0.025 (0.114)	-0.039 (0.118)	0.326 (0.108) **	-0.154 (0.109)
p for trend		<0.001	0.252	0.130	0.091	<0.001	0.305
FAMILY INCOME							
>2000 €	2738	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)
1200-2000 €	598	0.183 (0.046) **	0.020 (0.047)	0.024 (0.049)	-0.079 (0.048)	0.149 (0.047) **	-0.048 (0.048)
<1200 €	480	0.188 (0.062) **	0.063 (0.063)	-0.021 (0.066)	-0.269 (0.064) ***	0.237 (0.063) ***	-0.051 (0.065)
p for trend		<0.001	0.329	0.920	<0.001	<0.001	0.321

Values are regression coefficients and reflect differences in z-scores (standard error) between a certain SES category and the reference group.
 # Gives number of infants per SES category that were included in the analyses of at least one temperament scale (maximum 10% less subjects per SES level).
¶ Fear was log transformed.
§ In contrast to all other scales, higher scores on Recovery from Distress indicate less temperamental problems.
† Adjusted for infant age and ethnicity, sociodemographic characteristics (maternal age, marital status), family stress (Long Lasting Difficulties, Family Assessment Device) and maternal psychological well-being (prenatal and postpartum psychopathology, Rosenberg Self-Esteem Scale, Lack of Confidence in Caretaking).
** Indicates a significant difference from the reference group, p-value < 0.05, ** p-value < 0.01, *** p-value < 0.001.*

TABLE 4. EFFECT OF ADJUSTING FOR EXPLANATORY VARIABLES ON THE ASSOCIATION BETWEEN MATERNAL EDUCATIONAL LEVEL AND TWO SELECTED IBQ-R SUBSCALES

LEVEL OF MATERNAL EDUCATION	N	BASIC MODEL (BM): ADJUSTED FOR INFANT AGE AND ETHNICITY	BM ADDITIONALLY ADJUSTED FOR SOCIO-DEMOGRAPHIC CHARACTERISTICS	BM ADDITIONALLY ADJUSTED FOR FAMILYSTRESS	BM ADDITIONALLY ADJUSTED FOR PSYCHOLOGICAL WELL-BEING	FULLY ADJUSTED MODEL
		ACTIVITY LEVEL				
V (highest)	1250	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)
IV	947	0.015 (0.041)	-0.023 (0.041)	-0.004 (0.041)	0.001 (0.040)	-0.033 (0.040)
III	1116	0.217 (0.040)***	0.123 (0.041)**	0.167 (0.040)***	0.179 (0.040)***	0.100 (0.041)*
II	397	0.290 (0.056)***	0.147 (0.058)*	0.236 (0.056)***	0.240 (0.056)***	0.123 (0.058)*
I (lowest)	221	0.380 (0.073)***	0.272 (0.074)***	0.312 (0.074)***	0.297 (0.073)***	0.213 (0.074)**
p for trend		<0.001	<0.001	<0.001	<0.001	<0.001
		DISTRESS TO LIMITATIONS				
V (highest)	1249	0 (reference)	0 (reference)	0 (reference)	0 (reference)	0 (reference)
IV	945	-0.066 (0.041)	-0.084 (0.041)*	-0.088 (0.041)*	-0.079 (0.040)	-0.097 (0.040)*
III	1119	-0.006 (0.040)	-0.053 (0.041)	-0.070 (0.040)	-0.049 (0.040)	-0.093 (0.041)*
II	396	-0.046 (0.056)	-0.123 (0.058)*	-0.122 (0.056)*	-0.105 (0.056)	-0.167 (0.058)**
I (lowest)	227	0.172 (0.073)*	0.111 (0.074)	0.083 (0.073)	0.081 (0.073)	0.032 (0.074)
p for trend		0.296	0.706	0.400	0.582	0.101

Values are regression coefficients and reflect differences in z-scores (standard error) between a certain educational level and the reference group, i.e. highest education.
** Indicates a significant difference from the reference group, p-value < 0.05, ** p-value < 0.01, *** p-value < 0.001.*
Sociodemographic characteristics: maternal age, marital status.
Family stress: Long Lasting Difficulties, Family Assessment Device.
Psychological well-being: prenatal and postpartum psychopathology, Rosenberg Self-Esteem Scale, Lack of Confidence in Caretaking.
Fully adjusted model: BM additionally adjusted for sociodemographic characteristics, family stress and maternal psychological well-being.

DISCUSSION

This population-based study showed that a lower socioeconomic status, as measured by various indicators, is associated with a more difficult temperament in six months old infants. The effect of SES on several dimensions of infant temperament could partially be explained by sociodemographic characteristics, family stress, and maternal psychological well-being.

A few studies have examined the association between SES and infant temperament in the past. Only Sameroff et al.[28] described, just like the present study, an unambiguous socioeconomic gradient across various temperament dimensions. Other researchers reported no association[25] or only exceptionally found a socioeconomic gradient and thus considered this as a chance finding[26 27]. The discrepancy between these earlier findings and our results may be explained by the use of different temperament measures. The previous studies assessed temperament

according to nine dimensions as postulated by Thomas and Chess[46], which substantially differ from the more recent IBQ-R scales with regard to composition and psychometric properties[47]. Furthermore, limited statistical power of the previous studies due to smaller sample sizes –between 96 and 772 infants– may also explain the inconsistent findings.[25-27]

The results of the current study are, however, in line with reports of higher rates of problem behaviour and a higher prevalence of psychopathology in children of lower SES families as compared to those from a higher socioeconomic class.[1-11] Studies distinguishing between internalizing and externalizing behavioural problems reported a socioeconomic gradient for both dimensions. However, the SES gradient seems to be most substantial for externalizing problems.[2-4] The present study did not assess externalizing behaviour, though, research has indicated that temperamental difficulties in Activity Level, Distress to Limitations, and Recovery from Distress are predictive of later externalizing problems.[16 17 20] We reported that the SES inequalities in two out of these three temperament scales were explained by maternal psychological well-being and family stress. This result is interesting against the background of, for instance, evidence by Campbell[48] that both maternal depression and the experience of life-events are associated with externalizing problems. Apparently, adverse familial circumstances are already influential early in life, causing relatively high levels of distress in infants of lower SES families possibly predisposing to externalizing behavioural disorders.

Research indicates that young children with relatively high scores on Fear and Duration of Orienting are more likely to develop internalizing behavioural difficulties in later life.[16 17 21] Other studies have reported that the socioeconomic gradient is present in internalizing behavioural problems, even though this gradient is somewhat less substantial than for externalizing problems.[2-4] Although it was not the objective of our study to compare the different temperament dimensions, it is noteworthy that we observed the strongest association between SES and infant temperament in the Fear dimension and not in the temperamental scales encompassed in the concept of externalizing behaviour. We carefully speculate that several explanations for this finding, which is seemingly in contrast to observations made by other study groups, are conceivable. Possibly, fear traits are already more prevalent early in life than externalizing features.[49] Alternatively, the discrepancy may also result from differences in psychometric properties, which were excellent for the Fear dimension in comparison with other IBQ-R scales, that are very good to moderate (e.g. Sadness).[36] However, as temperament and behaviour remain different constructs, caution is needed in generalizing the results from the present study.

The Sadness dimension of the IBQ-R was introduced only recently.[36] Consequently, there are no studies of the relation between Sadness and later behavioural problems. Studies of infant temperament using different temperament measures found no association between SES and infants' mood, with the exception of one study.[25-28] In contrast to our observations, Sameroff *et al.*[28] reported a more negative mood, instead of a more positive mood, among infants of lower SES families as

compared to those from a higher socioeconomic class. Possibly, our observations are a chance finding. On the other hand, it is well known that symptoms of depression are not easily recognized in young children.[50] Finally, the association may also reflect the poor validity of the IBQ-R Sadness scale. Items like "Did your baby *seem sad* when the caregiver was gone for an unusually long period of time?" may be prone to subjective judgement. This notion is further supported by the low inter-rater agreement for Sadness as compared to other IBQ-R scales.[36]

In contrast to other scales, the SES gradient in Activity Level and Fear were not explained in the present study. Several explanations are conceivable. Firstly, we were able to account for selected explanatory mechanisms only. Factors like nutrition and sleeping patterns could also explain part of the SES inequalities in temperament. A second explanation for the strong relation between SES and Activity Level and Fear scores may be embedded in the presumed constitutional basis of temperament. Estimates of heritability suggest that genetic differences among individuals account for approximately 20 to 60% of the variability in temperament within a population.[17] Therefore, it seems plausible that environmental factors and proxies for heritability, such as maternal psychological well-being, cannot explain all temperamental variation between SES groups. Genetic factors could explain the observed SES inequalities if gene variations are associated with temperament and are differentially distributed across SES groups. This is not implausible considering mechanisms of social differentiation;[9 51] several temperament and personality characteristics, such as extraversion and conscientiousness, are related to educational attainment and career success. Most likely, genetic variations underlying these characteristics are more prevalent among certain SES levels.

The present study examined the association between multiple indicators of SES and infant temperament, rather than a single indicator or composite indices of SES. Of the different SES measures, maternal occupational status seemed to have the least consistent relation with infant temperament. Apparently, having children diminishes the variation in maternal occupational status, making it a less good measure of SES. The effects of paternal education on Distress to Limitations and Recovery from Distress were less concordant with the results of other SES indicators. Not unlikely this reflects selection effects, as information on paternal education was available for much less participants. Overall, the different indicators of SES yielded the same results suggesting that maternal and paternal education, maternal occupational status, and family income represent approximately the same construct of SES inequality in The Netherlands.

STRENGTHS AND LIMITATIONS

The strengths of the present study are the large number of participating infants and mothers, its population based design, and the information on numerous potential explanatory factors. However, our research has several limitations. Firstly, our non-response analyses indicated that data on infant temperament were more complete in infants of higher educated, non-single, and older mothers of Dutch ethnicity. This selective attrition resulted in an under-representation of infants

of the most disadvantaged groups, who are at increased risk for temperamental problems.[17] This could have affected our results if the relation between SES and infant temperament differed between responding and non-responding families. Secondly, infant temperament was assessed using an adapted version of the IBQ-R. A major modification was the reduction of the answering categories to a three-point scale. This adaptation may have decreased power to detect statistically significant SES differences in temperament scores. Finally, the objectivity of a maternal report of infant temperament is discussed.[52-54] A maternal report of infant behaviour may reflect infant as well as maternal characteristics.[53] However, the IBQ-R was designed to reduce the influence of maternal bias by inquiring about concrete infant behaviours rather than asking mothers to make abstract judgements.[36] Moreover, maternal perceptions of infant behaviour tend to be predictive of later child characteristics.[55 56]

CONCLUSION

In conclusion, socioeconomic inequalities in temperament were identified early, in infants only six months of age. These inequalities in infant temperament are likely precursors of the socioeconomic gradient in behaviour in later life. Tackling SES inequalities in mental health should thus start with early interventions. As some of the factors that explained a more difficult temperament of infants in low SES families, like single motherhood, family stress, and maternal psychopathology, are either preventable or amendable, these could be targets of intervention strategies.

REFERENCES

1. Caspi A, Taylor A, Moffitt TE, Plomin R. Neighborhood deprivation affects children's mental health: environmental risks identified in a genetic design. *Psychol Sci.* 2000;11(4):338-42.
2. Kahn RS, Wilson K, Wise PH. Intergenerational health disparities: socioeconomic status, women's health conditions, and child behavior problems. *Public Health Rep.* 2005;120(4):399-408.
3. Kalff AC, Kroes M, Vles JS, Hendriksen JG, Feron FJ, Steyaert J, et al. Neighbourhood level and individual level SES effects on child problem behaviour: a multilevel analysis. *J Epidemiol Community Health.* 2001;55(4):246-50.
4. Reijneveld SA, Brugman E, Verhulst FC, Verloove-Vanhorick SP. Area deprivation and child psychosocial problems–a national cross-sectional study among school-aged children. *Soc Psychiatry Psychiatr Epidemiol.* 2005;40(1):18-23.
5. Maughan B, Collishaw S, Meltzer H, Goodman R. Recent trends in UK child and adolescent mental health. *Soc Psychiatry Psychiatr Epidemiol* 2008;43(4):305-10.
6. Tick NT, van der Ende J, Verhulst FC. Ten-year trends in self-reported emotional and behavioral problems of Dutch adolescents. *Soc Psychiatry Psychiatr Epidemiol* 2008;43(5):349-55.
7. Bradley RH, Corwyn RF. Socioeconomic status and child development. *Annu Rev Psychol.* 2002;53:371-99.
8. Ford T, Goodman R, Meltzer H. The relative importance of child, family, school and neighbourhood correlates of childhood psychiatric disorder. *Soc Psychiatry Psychiatr Epidemiol* 2004;39(6):487-96.
9. Johnson JG, Cohen P, Dohrenwend BP, Link BG, Brook JS. A longitudinal investigation of social causation and social selection processes involved in the association between socioeconomic status and psychiatric disorders. *J Abnorm Psychol.* 1999;108(3):490-9.
10. Scahill L, Schwab-Stone M, Merikangas KR, Leckman JF, Zhang H, Kasl S. Psychosocial and clinical correlates of ADHD in a community sample of school-age children. *J Am Acad Child Adolesc Psychiatry* 1999;38(8):976-84.
11. Cicchetti D, Toth SL. The development of depression in children and adolescents. *Am Psychol.* 1998;53(2):221-41.
12. Larsson HJ, Eaton WW, Madsen KM, Vestergaard M, Olesen AV, Agerbo E, et al. Risk factors for autism: perinatal factors, parental psychiatric history, and socioeconomic status. *Am J Epidemiol.* 2005;161(10):916-25; discussion 926-8.
13. Kalff AC, Kroes M, Vles JS, Bosma H, Feron FJ, Hendriksen JG, et al. Factors affecting the relation between parental education as well as occupation and problem behaviour in Dutch 5- to 6-year-old children. *Soc Psychiatry Psychiatr Epidemiol* 2001;36(7):324-31.
14. Bates JE. Concepts and measures of temperament. In: Kohnstamm GA, Bates JE, Rothbart MK, editors. *Temperament in childhood.* Chichester: John Wiley & Sons., 1989:3-25.
15. Scarpa A, Raine A, Venables PH, Mednick SA. The stability of inhibited/uninhibited temperament from ages 3 to 11 years in Mauritian children. *J Abnorm Child Psychol* 1995;23(5):607-18.
16. Rothbart MK, Ahadi SA, Evans DE. Temperament and personality: origins and outcomes. *J Pers Soc Psychol* 2000;78(1):122-35.
17. Saudino KJ. Behavioral genetics and child temperament. *J Dev Behav Pediatr* 2005;26(3):214-23.
18. Frick PJ. Integrating research on temperament and childhood psychopathology: its pitfalls and promise. *J Clin Child Adolesc Psychol* 2004;33(1):2-7.
19. Lahey BB. Commentary: role of temperament in developmental models of psychopathology. *J Clin Child Adolesc Psychol* 2004;33(1):88-93.
20. Caspi A, Henry B, McGee RO, Moffitt TE, Silva PA. Temperamental origins of child and adolescent behavior problems: from age three to age fifteen. *Child Dev.* 1995;66(1):55-68.

21. Schwartz CE, Snidman N, Kagan J. Adolescent social anxiety as an outcome of inhibited temperament in childhood. *J Am Acad Child Adolesc Psychiatry* 1999;38(8):1008-15.
22. Matheny AP. Temperament and cognition: relations between temperament and mental test scores. In: Kohnstam GA, Rothbart MK, editors. *Temperament in childhood*: Chichester, New York, Brisbane, Toronto, Singapore: John Wiley & Sons., 1989.
23. Sajaniemi N, Hakamies-Blomqvist L, Makela J, Avellan A, Rita H, von Wendt L. Cognitive development, temperament and behavior at 2 years as indicative of language development at 4 years in pre-term infants. *Child Psychiatry Hum Dev* 2001;31(4):329-46.
24. Sanson A, Hempshill SA, Smart D. Connections between Temperament and Social Development: A Review. *Social Dev.* 2004;13(1):142-170.
25. Matheny AP, Wilson RS, Thoben AS. Home and Mother: Relations with Infant Temperament. *Dev Psychol.* 1987;23(3):323-331.
26. Maziade M. Infant temperament: SES and Gender Differences and Reliability of Measurement in a Large Quebec Sample. *Merrill-Palmer Quarterly.* 1984;30(2):213-26.
27. Persson-Blennow I, McNeil TF. Temperament characteristics of children in relation to gender, birth order, and social class. *Am J Orthopsychiatry.* 1981;51(4):710-4.
28. Sameroff AJ, Seifer R, Elias PK. Sociocultural variability in infant temperament ratings. *Child Dev* 1982;53(1):164-73.
29. Campbell SB. Behavior problems in preschool children: a review of recent research. *J Child Psychol Psychiatry.* 1995;36(1):113-49.
30. Eskenazi B, Castorina R. Association of prenatal maternal or postnatal child environmental tobacco smoke exposure and neurodevelopmental and behavioral problems in children. *Environ Health Perspect* 1999;107(12):991-1000.
31. Linnet KM, Dalsgaard S, Obel C, Wisborg K, Henriksen TB, Rodriguez A, et al. Maternal lifestyle factors in pregnancy risk of attention deficit hyperactivity disorder and associated behaviors: review of the current evidence. *Am J Psychiatry* 2003;160(6):1028-40.
32. Braveman PA, Cubbin C, Egerter S, Chideya S, Marchi KS, Metzler M, et al. Socioeconomic status in health research: one size does not fit all. *JAMA.* 2005;294(22):2879-88.
33. Jaddoe VW, Mackenbach JP, Moll HA, Steegers EA, Tiemeier H, Verhulst FC, et al. The Generation R Study: Design and cohort profile. *Eur J Epidemiol.* 2006;21(6):475-84.
34. *Standaard Onderwijsindeling 2003, Voorburg/Heerlen.* Statistics Netherlands, 2004a.
35. *Standaard Beroepenclassificatie 1992, Voorburg/Heerlen.* Statistics Netherlands, 1992.
36. Gartstein M, Rothbart M. Studying infant temperament via the Revised Infant Behavior Questionnaire. *Infant Behavior and Development.* 2003;26:64-86.
37. Roza SJ, PA VANL, Jaddoe VW, Steegers EA, Moll HA, Mackenbach JP, et al. Intrauterine Growth and Infant Temperamental Difficulties: The Generation R Study. *J Am Acad Child Adolesc Psychiatry* 2008;47(3):264-272.
38. MacKinnon DP, Krull JL, Lockwood CM. Equivalence of the mediation, confounding and suppression effect. *Prev Sci* 2000;1(4):173-81.
39. Hendriks A, Ormel J, Willige Gvd. Long lasting difficulties measured with a self-assessment questionnaire and semi-structured interview: a theoretical and empirical comparison [in Dutch]. *Gedrag Gezondh.* 1990;18:273-283.
40. Miller IW, Epstein NB, Bishop DS, Keitner GI. The McMaster Family Assessment Device: Reliability and validity. *J Marital Fam Ther.* 1985;11:345-356.
41. Derogatis LR. *Brief Symptom Inventory (BSI): Administration, scoring and procedures. Manual, third edition*. Minneapolis, MN, USA, 1993.
42. Rosenberg M. *Society and the adolescent child.* Princeton, NJ: Princeton University Press, 1965.

43. Brazelton TB, Nugent JK. *Neonatal Behavioral Assessment Scale*: 3rd edition. Mac Keith Press. Cambridge University Press., 1995.
44. Cohen J. *Statistical power analysis for the behavioral sciences.* 2nd ed. ed. Hillsdale, NJ.: Lawrence Earlbaum Associates., 1988.
45. Harrell Jr. FE. *Regression Modeling Strategies: With Applications to Linear Models, Logistics Regression, and Survival Analysis*. New York, USA: Springer-Verlag New York, Inc., 2001.
46. Thomas A, Chess S. *Temperament and development.* New York, USA.: New York University Press., 1977.
47. Rothbart MK, Posner MI. Temperament, Attention, and Developmental Psychopathology. In: Cicchetti D, Cohen DJ, editors. *Developmental Psychopathology. Volume two: Developmental Neuroscience.* Hoboken, New Yersey: John Wiley & Sons, Inc., 2006:465-501.
48. Campbell SB. Hard-to-manage preschool boys: externalizing behavior, social competence, and family context at two-year followup. *J Abnorm Child Psychol* 1994;22(2):147-66.
49. Egger HL, Angold A. Common emotional and behavioral disorders in preschool children: presentation, nosology, and epidemiology. *J Child Psychol Psychiatry* 2006;47(3-4):313-37.
50. Carlson GA. The challenge of diagnosing depression in childhood and adolescence. *J Affect Disord* 2000;61 Suppl 1:3-8.
51. Mackenbach JP. Genetics and health inequalities: hypotheses and controversies. *J Epidemiol Community Health* 2005;59(4):268-73.
52. Hane AA, Fox NA, Polak-Toste C, Ghera MM, Guner BM. Contextual basis of maternal perceptions of infant temperament. *Dev Psychol.* 2006;42(6):1077-88.
53. Leerkes A, Crockenberg S. The impact of maternal characteristics and sensitivity on the concordance between maternal reports and laboratory observations of infant negative emotionality. *Infancy.* 2003;4:517-539.
54. Seifer R, Sameroff AJ, Barrett LC, Krafchuk E. Infant temperament measured by multiple observations and mother report. *Child Dev* 1994;65(5):1478-90.
55. Oberklaid F, Sanson A, Pedlow R, Prior M. Predicting preschool behavior problems from temperament and other variables in infancy. *Pediatrics.* 1993;91(1):113-20.
56. Olson S, Bates J, Bayles K. Predicting Long-Term Developmental Outcomes From Maternal Perceptions of Infant and Toddler Behavior. *Infant Behavior and Development.* 1989;12:77-92.

CHAPTER **3.2**

National origin and behavioural problems of toddlers: the role of family risk factors and maternal immigration characteristics

ABSTRACT

In many societies the prevalence of behavioural problems in school-aged children varies by national origin. We examined the association between national origin and behavioural problems in 1½-year-old children. Data on maternal national origin and the Child Behavior Checklist for toddlers (n=4943) from a population-based cohort in the Netherlands were used. Children from various non-Dutch backgrounds all had significantly higher mean behavioural problem scores (e.g. 18.4 in Dutch vs. 28.1 in Antillean children, difference=9.7, $p<0.001$). After adjustment for family risk factors, e.g. family income, the differences attenuated, but remained statistically significant. Non-Dutch mothers with immigration risk factors, such as older age at migration or not having good Dutch language skills, reported significantly more behavioural problems in their offspring. In conclusion, the present study indicated more behavioural problems in immigrant toddlers from various backgrounds. Researchers and policymakers aiming to tackle disparities in behavioural problems should take into account that risks associated with national origin are intertwined with unfavourable family and immigration characteristics.

INTRODUCTION

During the past decades, the number of non-Western individuals moving to Western countries has increased rapidly due to economical factors and political conflicts in other parts of the world. Whereas a large group came as immigrants, another group entered European countries as migrant workers of whom many later decided to stay and thereby became immigrants. Immigrants of diverse ethnic backgrounds living in Europe have been reported to be at high risk for mental health problems, such as depression, anxiety disorders, and schizophrenia.[1] The risk is seen among immigrants originating from non-Western countries, and to a lesser extent in those migrating within Europe. Research on this topic in school-aged children and adolescents, however, provided mixed results. Studies indicated that immigrant children of diverse national backgrounds tend to exhibit more behavioural problems than non-immigrants as measured with behaviour checklists completed by parents.[2-6] Conversely, other studies in Western countries showed similar levels of problem behaviour in immigrant and native children,[7 8] and it has even been found that immigrants report lower rates of behavioural problems in their offspring than parents of native children.[9 10] In general, many of the studies of behavioural problems among immigrant children were hampered by small sample sizes.[3 5 8 10] Moreover, the restriction to immigrants originating from one country only and the study of immigrants of different backgrounds as one group limits generalizability.[2 5 6 8-10] Finally, previous studies often controlled marginally for confounders,[2-5 9] while these factor possibly elucidate the association between immigrant status and mental health.

Well known risk factors of child behavioural problems,[11 12] such as low socioeconomic position, single parenthood, and parental psychopathology, possibly explain the elevated levels of behavioural problems among immigrant children. For instance, many immigrants end up in the lower socioeconomic strata of a host country and experience financial problems, largely due to language difficulties or lack of adequate education.[13] Generally, studies on parent reported behavioural problems among immigrant children control for socioeconomic status, but other family risk factors are rarely accounted for. Hence, their role in the association between national origin and behavioural problems remains unknown. Alternatively, the increased risk of mental health problems among first-generation adult and adolescent immigrants has been ascribed to characteristics of the immigration process. Immigration causes stress due to loss of the familiar environment and adaptation to a new situation.[13 14] Moreover, immigrants may find it hard to identify with the host culture and may experience rejection by the mainstream society. For instance, a study among Moroccan adolescents in the Netherlands indicated that perceived discrimination predicted externalizing behavioural problems.[15] However, it is largely unknown how characteristics of the immigration process as experienced by immigrant parents affect behaviour in the offspring. Intergenerational effects of parental immigration characteristics may be involved; a study among Asian immigrants, for instance, indicated that the refugee process of parents was strongly re-

lated to violent behaviour in their children.[16] So, both immigration characteristics and family risk factors should be taken into account to disentangle the underlying mechanisms in the association between national origin and behavioural problems in children. Furthermore, it is important to study immigrants originating from different countries. Finally, the association between national origin and behavioural problems has, to our knowledge, not been examined in preschool children, while growing evidence suggests that behavioural problems early in life tend to persist into later ages and predict adverse outcomes during childhood.[17]

We examined the association between maternal national origin and behavioural problems in toddlers of 1½ year old in a large, multi-ethnic cohort study. While the importance of ethnic minority as a risk factor for problem behaviour in children is well-recognized, research that may elucidate the mechanisms underlying the poor mental health among immigrant children is needed. Without insight into these mechanisms prevention is hardly possible and treatment may be less effective. Therefore, we also investigated whether family risk factors can explain the relation between national origin and behavioural problems. Moreover, we explored the association of maternal immigration characteristics, e.g. generational status, Dutch language skills, and feelings of acceptance by Dutch natives, with child behaviour. Based on the literature among immigrant children from former colonies[6] and among adolescent immigrants[2 4] living in the Netherlands, we hypothesize that toddlers of non-Western origin have more behavioural problems than Dutch toddlers. We assume that part of these behavioural problems is due to family risk factors and adverse maternal immigration characteristics, such as lack of good Dutch language skills and not feeling at home in the Netherlands. We also hypothesize that toddlers of non-Dutch European descent display the same level of behavioural problems as Dutch toddlers, because immigration within Europe probably requires less adaptability and causes less stress than intercontinental immigration. Moreover, we assume that the socioeconomic status of non-Dutch European and Dutch families is relatively similar.

METHODS

DESIGN

This study was embedded in Generation R, a population-based cohort from fetal life onwards.[18] Briefly, all pregnant women living in Rotterdam, the Netherlands, with an expected delivery date between April 2002 and January 2006 were invited to participate. The participation rate was estimated at 61% (based on cohort years 2003 and 2004: of the 8494 live births in the study area, 5189 participated). Written informed consent was obtained from all participants. The Medical Ethical Committee of the Erasmus Medical Centre, Rotterdam, has approved the study.

Questionnaires were available in three languages, e.g. the behaviour checklist was filled out in Dutch (n=4813), in English (n=14), and in Turkish (n=116). For those not able to read these languages, research assistants helped filling out the

questionnaires. We contracted English, French, Arabic or Berber (Moroccan), Portuguese (Cape Verdian), and Turkish speaking research assistants to communicate with the participants.

POPULATION FOR ANALYSIS

Full consent for the postnatal phase of the Generation R Study was obtained from 7295 children and their mothers. Those without information on maternal national origin (n=603) and child behaviour at 18 months (n=1719) were excluded. The response rate for the behaviour questionnaire was 74% (4973 / 6692). Due to small numbers, 30 mothers of different national origins were additionally excluded (i.e. USA n=11, Australia n=3, Japan n=3, and other n=13), yielding a sample size of 4943 mother-child dyads for the present study. The analyses of immigration characteristics were restricted to the non-Dutch groups (n=1753). In these analyses the study population varies slightly due to missing data on the individual items.

NATIONAL ORIGIN

Maternal national origin was based on country of birth of the mothers' parents, which was assessed by questionnaire during pregnancy. In accordance with Statistics Netherlands,[19] we classified a mother as non-Dutch if one of her parents was born abroad. If both parents were born abroad, the country of birth of the mothers' mother decided on maternal national origin. Among non-Dutch mothers in this study, we identified persons of European (n=406) and non-Western (n=1347) origins. The non-Western group consisted of: Cape Verdian (n=110), Dutch Antillean (n=84), Indonesian (n=190), Moroccan (n=164), Surinamese (n=278), Turkish (n=301), and Other non-Western (n=220). A large number of immigrants are from former Dutch colonies, i.e. Dutch Antilles, Indonesia, and Suriname. Others, from Cape Verdian, Morocco, and Turkey have an immigration history starting in the 1960s when 'guest workers' came to the Netherlands. More recently, immigration occurred mostly for marital reasons.

BEHAVIOURAL PROBLEMS

At the age of 1½ year, child behaviour was assessed using the Dutch version of the Child Behavior Checklist for toddlers (CBCL/1½ -5). The CBCL/1½ -5 is a 99-item questionnaire designed to obtain ratings of behaviour and emotional problems by parents of 1½- to 5-year-old children.[20] Parents are asked to rate the occurrence of their child's behaviour within the past two months on a scale from 0 (not true) to 2 (often true). In 95% of the children, the CBCL/1½ -5 was filled out by the mother. The CBCL/1½ -5 includes a Total problems score, which is the sum of all items, and two broadband scales. The Internalizing scale (36 items) comprises problems such as anxiety, sadness and withdrawn behaviour. The Externalizing scale (24 items) involves attention problems and aggressive behaviour. Higher scores on the CBCL scales indicate more behavioural problems. In this study, mean scores and differences in mean scores are presented. To give an indication of clinical relevance, we also present the percentage of children with a score in the borderline/clinical

range in TABLE 2. The cut off point for this score is based on the 83rd percentile of a Dutch norm group.[21]

Good reliability and validity have been reported for the English and Dutch CBCL/1½ -5.[20 21] More specifically, the construct validity of the CBCL/1½ -5 problem scales was supported by concurrent and predictive associations with a variety of other measures, such as other parental reports for toddlers' behaviour, referral to mental health facilities, later behavioural problems, and psychiatric diagnoses using the Diagnostic and Statistical Manual.[17 20] The cross-cultural validation has not yet been ascertained, but CBCL versions for other age ranges showed high cross-cultural validity.[22] To check the validity of the factor structure within the different national origins of our study population, we calculated Cronbach's alphas for the Internalizing and Externalizing CBCL/1½ -5 scales. The alphas are presented in TABLE 1 and range between 0.75 (Dutch, Externalizing problems) and 0.89 (other non-Western, Internalizing problems), indicating acceptable to high internal consistencies.

TABLE 1. INTERNAL CONSISTENCIES OF CBCL SCALES PER NATIONAL ORIGIN

		CRONBACH'S ALPHAS	
MATERNAL NATIONAL ORIGIN	**N**	**INTERNALIZING PROBLEMS**	**EXTERNALIZING PROBLEMS**
Dutch	3190	0.763	0.751
European	406	0.778	0.787
All Non-Western	1347	0.856	0.818
Non-Western subgroups:			
Antillean	84	0.856	0.771
Cape Verdian	110	0.858	0.756
Indonesian	190	0.862	0.770
Moroccan	164	0.841	0.850
Surinamese	278	0.833	0.817
Turkish	301	0.807	0.816
Other Non-Western	220	0.894	0.845

IMMIGRATION CHARACTERISTICS

The immigration characteristics were assessed during pregnancy. Generational status of mothers with a non-Dutch national origin was based on their own country of birth: foreign-born mothers were classified as 'first generation', and mothers born in the Netherlands, while having non-native parents, were classified as 'second generation'. Of the first generation mothers, age at immigration to the Netherlands was dichotomized into '0 -15 years old' (42%) and '≥16 years old' (58%). For those in the first category it was mandatory to attend school in the Netherlands, whereas those immigrating at age 16 or older were not obliged to attend school anymore. Mothers were asked to rate their Dutch speaking, reading and writing skills on three separate 5-point scales ranging from 'not at all' (1) to 'good' (5). This information was summed into general 'Dutch language skills' (1-9, not good; 10-

14, reasonable; 15, good). Cultural identity was assessed with the item "Feels part of…" (Dutch culture; own national culture; both cultures; neither of the cultures) and feelings of acceptance were assessed with the item "Feels accepted by Dutch natives" (agree; neither agree, nor disagree; disagree). Items were based on questions in an international study on acculturating youth (ICSEY).[23]

COVARIATES

Family risk factors were regarded as possible explanatory variables in the association between national origin and child behavioural problems. Family risk factors were assessed by questionnaire during pregnancy. The family risk factors included maternal age, marital status (married/cohabiting, single) and smoking habits during pregnancy (yes, no). Maternal psychopathology was assessed using the Brief Symptom Inventory,[24] a validated self-report questionnaire which consists of 53 positive and negative self-appraisal statements. The internal consistency for the Global Severity Index, the overall score of the BSI, in this sample was α=0.96, which indicates high construct reliability. Furthermore, maternal educational level was defined by the highest attained educational level and classified into 3 categories according to the definition of Statistics Netherlands [25]: low (primary school, lower vocational training, intermediate general school, 3 years general secondary school), mediate (>3 years general secondary school; intermediate vocational training; 1st year higher vocational training), and high (higher vocational training, Bachelor's degree, higher academic education and PhD). Family income, defined by the total net month income of the household, was categorized as '<1200 €' (below social security level), '1200-2000 €' and '>2000 €' (more than modal income). We defined parity as the number of life births the mothers delivered before the birth of the participating child (0, ≥1).

We also adjusted the analyses for gender, birth weight, gestational age at birth and age of the children. Although these covariates are probably not on the causal pathway between national origin and child behaviour, they might confound the associations. Information on these covariates was obtained from the medical records completed by community midwives and obstetricians.

STATISTICAL ANALYSES

All statistical analyses were performed using the Statistical Package of Social Sciences version 11.0 for Windows (SPSS Inc, Chicago, IL, USA). We studied the association between national origin (Dutch, European and non-Western) and several child and maternal characteristics with χ^2-tests, ANOVA's, or Kruskal-Wallis tests. The tests were chosen depending on the nature of the variables (see footnote TABLE 2). Next, analyses of variance were used to calculate unadjusted mean behavioural problem scores per national origin and to detect differences between each national origin and the Dutch reference group. Subsequently, using multivariate linear regression analyses, we studied the association between national origin and CBCL scores adjusted for family risk factors. Since gestational age at birth and child age did not meaningfully change the effect estimates of the as-

sociation between national origin and behavioural problems (i.e. <5% change in estimates), these covariates were not included in the models.[26] For each variable in the full model, the R^2 is displayed to indicate the proportion of variability of the behavioural problem score that is accounted for by this variable. The R^2 of a variable was calculated by repeating the regression analyses excluding that specific variable: R^2 model including all variables – R^2 of model excluding a specific variable. Next, we examined the association between maternal immigration characteristics and behavioural problems in the non-Dutch population. Due to relatively small numbers in some strata of national origin, we combined all mother-child dyads of non-Western origin. In both the European and non-Western groups, we performed univariate analyses of variance to calculate the mean behavioural problem scores per category of the immigration characteristics. We also report the R^2 of each immigration characteristic as generated by the ANOVA's. Based on the univariate associations between the immigration characteristics and behavioural problem scores, the following categories of the immigration characteristics were labelled as 'risk': first generation immigrant, ≥16 years at immigration, no good or reasonable Dutch language skills, feeling part of only own national culture or feeling part of neither Dutch nor own national culture, and disagreeing or neither agreeing nor disagreeing with the statement 'feels accepted by Dutch natives'. A risk index was calculated by summing the amount of risk immigration characteristics per participant, which generated an index ranging from 0 (no risk) to 5 (highest risk on immigration characteristics). Finally, both in the European and non-Western groups, the association between the immigration risk index and behavioural problems was assessed using linear regression analyses with the Dutch as reference. The analyses were performed with and without adjusting for the family risk factors. Missing values of covariates were replaced by the median (categorical or non-normally distributed continuous variables) or the mean (normally distributed continuous variables).

NON-RESPONSE ANALYSES

Within the Dutch subgroup, mothers with missing data on their children's behaviour at 18 months (n=629) were compared with mothers who filled out the CBCL/1½ - 5 (n=3190). Data on behaviour was more often missing in mothers who were lower educated (χ^2=187; df=2, p<0.001), single parent (χ^2=38; df=1; p<0.001), and younger (F-test=94; df=1; p<0.001) as compared to mothers who filled out the behaviour questionnaire. Similarly, Surinamese mothers with missing data on the CBCL (n=276) were also more often lower educated (χ^2=42; df=2, p<0.001), single parent (χ^2=16; df=1; p<0.001), and younger (F-test=480; df=1; p<0.001) than mothers of Surinamese descent who filled out the questionnaire (n=278). The non-response analyses in the other national origins resulted in the same pattern: non-responders were more often lower educated, single parent, and younger than mothers who filled out the behavioural questionnaires.

TABLE 2. CHARACTERISTICS OF MOTHERS AND THEIR CHILDREN BY MATERNAL NATIONAL ORIGIN

	N	DUTCH (N=3190)	OTHER EUROPEAN (N=406)	NON-WESTERN[a] (N=1347)
Child characteristics				
Gender (% boys)	4892	49.9	47.4	49.6
Age (months)	4936	18.4 (1.1)	18.4 (1.1)	18.6 (1.2) ***
Gestational age at birth (weeks)	4942	40.0 (26.7–43.4)	40.0 (29.6–43.0)	39.9 (27.1–43.4) ***
Birth weight (grams)	4888	3511 (551)	3474 (537)	3336 (545) ***
Children with CBCL borderline/clinical score:				
Total problems (%)	4943	4.5	11.8 ***	18.9 ***
Internalizing problems (%)	4943	11.1	20.9 ***	31.9 ***
Externalizing problems (%)	4943	5.3	8.6 **	10.4 ***
Maternal characteristics				
Educational level: high (%)	2747	65.8	67.0	33.6 ***
mediate (%)	1350	24.3	24.6	35.3 ***
low (%)	769	9.9	8.4	31.0 ***
Family income: ›2000 €	3800	86.3	78.1 ***	54.1 ***
1200-2000 €	660	10.3	14.8 ***	20.1 ***
‹1200 €	483	3.4	7.1 ***	25.8 ***
Marital status (% single)	4846	5.4	6.0	18.1 ***
Age (years)	4943	32.1 (4.0)	31.6 (4.4) *	29.4 (5.6) ***
Parity (% nulli)	4783	60.3	61.0	54.8 **
Psychopathology symptoms (score)	3965	0.12 (0.00–2.63)	0.17 (0.00–2.25) ***	0.22 (0.00–2.86) ***
Smoking during pregnancy (% yes)	4160	22.4	23.5	24.7
Immigration characteristics of mothers				
Generational status				
Second generation (%)	650		38.3	36.8
First generation (%)	1100		61.7	63.2
Age at immigration of first generation immigrants[b]				
0 - 15 years old (%)	381		10.3	28.0 ***
≥ 16 years old (%)	573		49.7	31.3 ***
Dutch language skills				
Good (%)	814		49.7	51.2
Reasonable (%)	478		30.0	29.8
Not good (%)	309		20.3	19.0
Cultural identity				
"Feels part of …"				
Dutch culture (%)	306		26.5	21.2 *
Dutch and own national culture (%)	582		44.9	42.2 *
Own national culture (%)	415		26.5	31.9 *
Neither Dutch nor own national culture (%)	55		2.1	4.7 *
Feelings of acceptance				
"Feels accepted by Dutch natives"				
Agree (%)	740		74.4	54.2 ***
Neither agree, nor disagree (%)	354		18.9	31.1 ***
Disagree (%)	160		6.7	14.6 ***

Values are percentages for categorical variables, means (standard deviation) for continuous normally distributed variables, and medians (100% range) for continuous non-normally distributed variables.
** p-value ‹0.05, ** ‹0.01, *** ‹0.001; p-values indicate statistical significant difference from Dutch group (maternal and child characteristics) or from Other European group (immigration characteristics) calculated by a 2 x 2 χ^2-test for categorical variables, a 2 group ANOVA for continuous normally distributed variables, or a 2 group Kruskal-Wallis test for continuous non-normally distributed variables. Comparisons for variables with more than two categories were also performed with separated 2 x 2 χ^2-tests using the lowest risk category (e.g. high educational level or feeling part of Dutch culture) as the reference for all other categories in order to obtain specific p-values per category. European or non-Western participants are compared to Dutch persons in separated analyses. [a] Included: Cape Verdian (n=110), Dutch Antillean (n=84), Indonesian (n=190), Moroccan (n=164), Surinamese (n=278), Turkish (n=301), and Other non-Western (n=220). [b] Only first generation immigrants included, as second generation immigrants were born in The Netherlands.*

RESULTS

Characteristics of the mother-child dyads are presented in TABLE 2. Both children of non-Dutch European (χ^2=39, df=1, p<0.001) and of non-Western descent (χ^2=249, df=1, p<0.001) were more likely to have a borderline / clinical Total Problems score than children with a Dutch background. Non-Western mothers were more often low educated (χ^2=448, df=1, p<0.001) and single (χ^2=182, df=1, p<0.001) as compared to their Dutch counterparts. In comparison to Dutch mothers, European (χ^2=38, df=1, p<0.001) and non-Western mothers (χ^2=280, df=1, p<0.001) reported more psychopathological symptoms. 74.4% of the European and 54.2% of the non-Western mothers felt accepted by the native Dutch. Other European and non-Western mothers did not differ with regard to generational status and Dutch language skills.

The mean scores on the CBCL scales per national origin are presented in TABLE 3. Compared to children of Dutch mothers, children of mothers from various non-Dutch backgrounds all had higher mean scores on the Total problems scale, indicating more behavioural problems. Particularly high behavioural problem scores were found in children of Cape Verdian and Turkish background (mean=32.4, 95% CI: 29.1–35.9; mean=30.9, 95% CI: 28.9–32.9, respectively).

TABLE 3. MEAN SCORES ON CBCL TOTAL PROBLEMS AND THE CBCL BROADBAND SCALES BY MATERNAL NATIONAL ORIGIN (N=4943)

MATERNAL NATIONAL ORIGIN	N	MEAN SCORES		
		TOTAL PROBLEMS	INTERNALIZING PROBLEMS	EXTERNALIZING PROBLEMS
Western				
Dutch	3190	18.4 (2.3)	3.3 (0.9)	8.8 (1.2)
European	406	22.5 (2.9) ***	4.5 (1.1) ***	10.0 (1.3) **
Non-Western				
Antillean	84	28.1 (3.7) ***	5.7 (1.3) ***	11.7 (1.6) ***
Cape Verdian	110	32.5 (2.9) ***	6.8 (1.1) ***	13.5 (1.2) ***
Indonesian	190	21.5 (2.5) **	3.7 (1.0)	9.9 (1.3) *
Moroccan	164	24.3 (4.4) ***	5.8 (1.7) ***	8.4 (1.5)
Surinamese	278	23.5 (3.0) ***	4.3 (1.2) ***	10.2 (1.4) **
Turkish	301	31.0 (3.2) ***	7.8 (1.4) ***	11.0 (1.3) ***
Other Non-Western	220	28.3 (4.5) ***	6.2 (1.6) ***	10.9 (1.2) ***
All Non-Western[a]	1347	26.7 (3.4) ***	5.7 (1.2) ***	10.6 (1.4) ***

Values are mean scores (standard deviations).
** p-value <0.05, ** <0.01, *** <0.001 for difference in mean score between a certain national origin and Dutch national origin.*
[a] *Analyses on national origin and CBCL scores repeated by including Antillean, Cape Verdian, Indonesian, Moroccan, Surinamese, Turkish, and Other Non-Western as one group ('all non-Western') in the analyses.*

TABLE 4 shows the association between maternal national origin and CBCL scores adjusted for family risk factors. The difference in mean score between Dutch and non-Dutch origins attenuated by adjustment for possible explanatory variables, but remained significant in all non-Dutch groups. For example, the difference in mean CBCL Total problem score between Dutch and Cape Verdian origin decreased

from 14.1 (mean Cape Verdian (32.5) - mean Dutch (18.4), p<0.001) to 8.92 (p<0.001) after adjustment for explanatory variables. Maternal psychopathology accounted for a large change in difference in mean Total problem score between children of Dutch and non-Dutch origins. The decrease in differences between Dutch and non-Dutch origins after adjustment for solely maternal psychopathology ranged from 14% (Antillean) to 33% (Moroccans) in the different non-Dutch groups. Marital status was an important explanatory variable in the Antillean (22% decrease in behavioural problems), Cape Verdian (17%) and Surinamese (28%) groups. Adjustment for maternal educational level or family income resulted in relatively small decreases in differences between Dutch and non-Dutch origins, i.e. decreases between 1% and 16%.

In children from virtually all non-Dutch backgrounds, the differences in mean scores with Dutch children were slightly more pronounced for the Internalizing problem scale than for the Externalizing problem scale. Of all variables included in the model, maternal national origin (R^2 = 0.033) and psychopathology (R^2 = 0.028) explained the highest percentage of variance in Total problems. The percentage of explained variance by all variables included in the model was moderately: Total problems R^2 = 0.138, Internalizing R^2 = 0.143, Externalizing R^2 = 0.073.

TABLE 4. ASSOCIATION BETWEEN MATERNAL NATIONAL ORIGIN AND CBCL SCORES ADJUSTED FOR FAMILY RISK FACTORS (N=4943)

VARIABLES INCLUDED IN MODEL	TOTAL PROBLEMS	R^2 [a]	INTERNALIZING PROBLEMS	R^2 [a]	EXTERNALIZING PROBLEMS	R^2 [a]
Intercept	23.6 (19.5, 27.7) ***		4.43 (3.20, 5.66) ***		12.1 (10.2, 13.9) ***	
Maternal national origin:		0.033		0.048		0.009
Dutch	0 (reference)		0 (reference)		0 (reference)	
European	3.79 (2.25,5.32) ***		1.13 (0.67, 1.59) ***		0.99 (0.32, 1.67) **	
Antillean	6.38 (3.07, 9.69) ***		1.59 (0.61, 2.58) **		1.58 (0.12, 3.03) *	
Cape Verdian	8.92 (5.97, 11.9) ***		2.19 (1.31, 3.07) ***		2.68 (1.38, 3.98) ***	
Indonesian	2.86 (0.69, 5.03) **		0.33 (-0.31, 0.98)		1.02 (0.06, 1.98) *	
Moroccan	4.30 (1.86, 6.75) **		2.29 (1.56, 3.02) ***		1.19 (0.11, 2.27) *	
Surinamese	2.13 (0.23, 4.04) *		0.39 (-0.18, 0.96)		0.26 (-0.58, 1.10)	
Turkish	9.46 (7.55, 11.4) ***		3.90 (3.33, 4.47) ***		0.93 (0.09, 1.77) *	
Other Non-Western	9.20 (7.15, 11.2) ***		3.05 (2.44, 3.66) ***		1.49 (0.58, 2.40) **	
Gender: boy	1.36 (0.53, 2.18) **	0.002	0.02 (-0.23, 0.27)	0.000	0.95 (0.58, 1.31) ***	0.005
Birth weight	0.00 (-0.001, 0.00)	0.000	0.00 (-0.00, 0.0001)	0.000	0.00 (0.00, 0.00)	0.001
Parity: nulliparity	1.20 (0.30, 2.10) **	0.001	0.29 (0.03, 0.56) *	0.001	0.37 (-0.02, 0.77)	0.001
Maternal age	-0.18 ***	0.002	-0.03 (-0.06, -0.002) *	0.001	-0.10 (-0.14, -0.05) ***	0.004
Marital status: single	3.95 (2.31, 5.59) ***	0.004	0.96 (0.47, 1.45) ***	0.003	1.65 (0.93, 2.37) ***	0.004
Maternal education: high	0 (reference)	0.003	0 (reference)	0.003	0 (reference)	0.001
mediate	0.86 (-0.16, 1.87)		0.09 (-0.21, 0.40)		0.24 (-0.21, 0.69)	
low	2.53 (1.17, 3.88) ***		0.80 (0.39, 1.20) ***		0.52 (-0.08, 1.11)	
Family income: >2000 €	0 (reference)	0.001	0 (reference)	0.003	0 (reference)	0.001
1200-2000 €	-0.53 (-1.81, 0.75)		-0.23 (-0.62, 0.15)		-0.03 (-0.78, 0.71)	
<1200 €	1.73 (0.04, 3.41) *		0.85 (0.35, 1.35) **		-0.35 (-0.92, 0.21)	
Maternal psychopathology	9.86 ***	0.028	2.73 (2.28, 3.19) ***	0.024	3.71 (3.04, 4.39) ***	0.023
Smoking during pregnancy: yes	0.38 (-0.71, 1.46)	0.000	0.45 (0.12, 0.77) **	0.001	-0.33 (-0.81, 0.15)	0.001

Values are regression coefficients.
** p-value <0.05, ** <0.01, *** <0.001.*
[a] Presented R^2 = R^2 of model including all variables - R^2 of model excluding one of the variables. E.g. the R^2 of 0.033 indicating the effect of national origin on Total problems is as follows: R^2 of model including all variables (0.138) - R^2 of model without national origin (0.105).

TABLE 5. MEAN SCORES ON CBCL TOTAL PROBLEMS BY MATERNAL IMMIGRATION CHARACTERISTICS

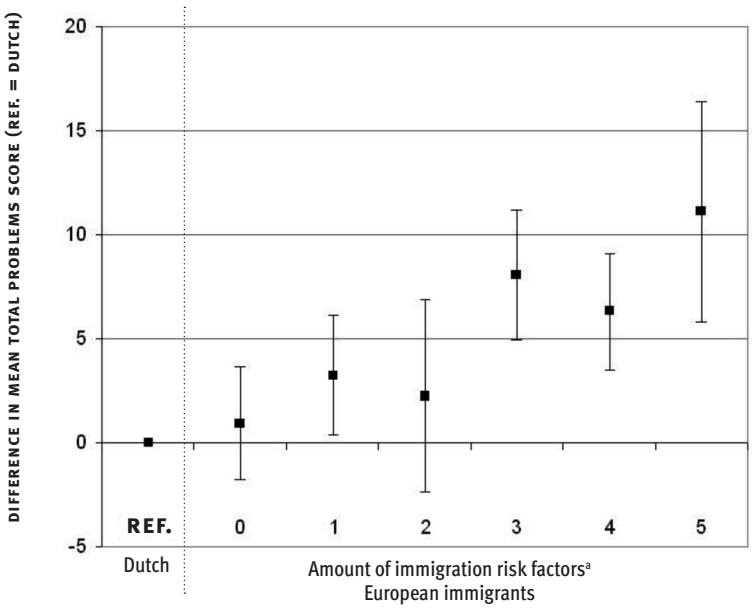
	MEAN TOTAL PROBLEM SCORES			
MATERNAL IMMIGRATION CHARACTERISTICS	**EUROPEAN (N=406)**	**R^{2b}**	**NON-WESTERN (N=1347)**	**R^{2b}**
Generational status:				0.008
Second	24.0 (16.3)	0.005	27.8 (17.2)	
First	26.2 (16.5)		31.4 (20.5) **	
Age at immigration of first generation immigrants[a]:				0.017
0 - 15 years old	22.2 (15.7)	0.016	28.4 (19.0)	
≥ 16 years old	27.7 (16.8)		33.2 (19.5) **	
Dutch language skills:	23.7 (16.1)	0.012	26.6 (16.7)	0.032
Good	27.0 (16.7)		31.9 (19.7) ***	
Reasonable	27.5 (17.3)		34.9 (21.8) ***	
Not good				
Cultural identity: *"Feels part of ..."*				0.033
Dutch culture	22.1 (15.2)	0.045	28.6 (18.3)	
Dutch and own national culture	25.5 (16.0)		26.5 (16.0)	
Own national culture	27.3 (16.8)		33.9 (21.2) **	
Neither Dutch nor own national culture	44.9 (17.5) *		35.4 (20.4) *	
Feelings of acceptance: *"Feels accepted by Dutch natives"*				0.017
Agree	24.6 (15.6)	0.018	27.5 (17.7)	
Neither agree, nor disagree	27.5 (16.2)		32.7 (19.0) ***	
Disagree	32.6 (20.5)		31.6 (20.3) *	

Values are mean scores (standard deviations) calculated by univariate ANOVA's.
** p-value <0.05, ** <0.01, *** <0.001 for difference in mean score between a certain category and the reference category. Reference categories for the separate immigration characteristics are: second generation, age at immigration 0-15 years, good Dutch language skills, feeling part of Dutch culture, or agreeing with 'feeling accepted by Dutch natives'.*
[a] Only first generation immigrants included, as second generation immigrants were born in The Netherlands.
[b] R^2 as displayed in the univariate ANOVA.

TABLE 5 shows the association between immigration characteristics of non-Dutch mothers and mean Total problem score in the offspring. First generation mothers had children with higher behavioural problem scores than mothers who were born in the Netherlands. This difference was only significant in mothers of non-Western descent (difference in European: 2.2, p=0.180; in non-Western: 3.6, p=0.001). Poor Dutch language skills of non-Western mothers were also associated with higher behavioural problem scores in toddlers, as was lack of feelings of acceptance by Dutch natives (see TABLE 5). Among children of non-Dutch European origin we observed the same tendencies as in the non-Western group, although these associations did not reach statistical significance due to a small sample size. The immigration characteristics were highly correlated with each other: the Spearman's rho ranged between 0.191 (feelings of acceptance and age at immigration, p<0.001) and 0.909 (generational status and age at immigration, p<0.001). Therefore, a risk index was calculated based on the maternal immigration characteristics that were associated with child behavioural problems. FIGURES 1 and 2 present the association between an accumulation of adverse immigration characteristics and child behavioural problems. European toddlers with 3-5 five immigration risks

have significantly higher Total problem scores than Dutch toddlers (FIGURE 1A); after adjustment for family risk factors, these differences between European and Dutch toddlers attenuate, but remain statistically significant (FIGURE 1B). Non-Dutch European children with a few immigration risks (0-2) do not have higher Total problem scores than toddlers of Dutch origin, this is especially apparent after adjustment for the family risk factors (FIGURE 1B). FIGURE 2A points out that, independently of the amount of immigration risks, toddlers of non-Western origin have a higher mean Total problem score than Dutch toddlers. The higher problem score among non-Western toddlers without any maternal immigration risk is explained by the family risk factors (adjusted difference=1.53, 95% CI: -0.28–3.35) (FIGURE 2B). The difference in Total problem scores between Dutch children and non-Western children with 1 or more immigration risks becomes smaller after adjustment, but remains statistically significant (FIGURE 2B).

FIGURE 1A. UNADJUSTED ASSOCIATION BETWEEN IMMIGRATION RISK INDEX[a] IN EUROPEANS AND CBCL TOTAL PROBLEMS



LEGEND OF FIGURES 1A, 1B, 2A AND 2B

Values are regression coefficients indicating differences in mean Total problem score between Dutch toddlers (reference) and toddlers of European or non-Western origin divided according to their amount of immigration risks (between 0 and 5).

[a] Based on TABLE 5*, the following categories of the immigration characteristics were labelled as 'risk': first generation, ≥16 years at immigration, no good Dutch language skills, feeling part of only own or of neither Dutch nor own national culture, and not agreeing with statement 'feels accepted by Dutch natives'*

[b] Adjusted for gender, birth weight, parity, marital status, family income, smoking during pregnancy, and maternal age, education, and psychopathology.

FIGURE 1B. ADJUSTED[b] ASSOCIATION BETWEEN IMMIGRATION RISK INDEX[a] IN EUROPEANS AND CBCL TOTAL PROBLEMS

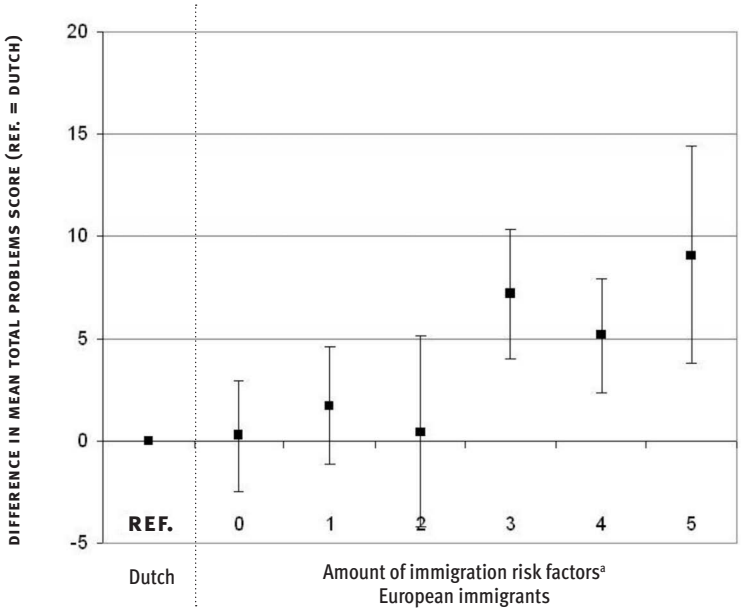


FIGURE 2A. UNADJUSTED ASSOCIATION BETWEEN IMMIGRATION RISK INDEX[a] IN NON-WESTERNS AND CBCL TOTAL PROBLEMS

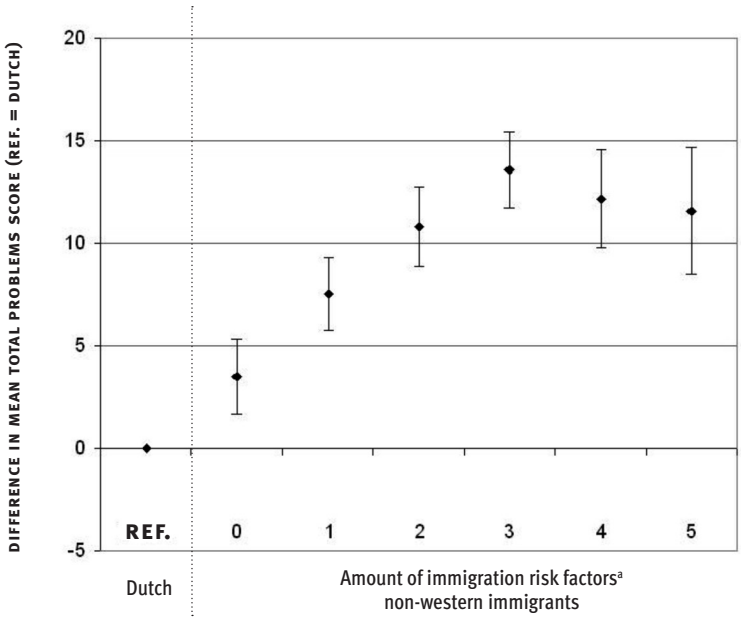
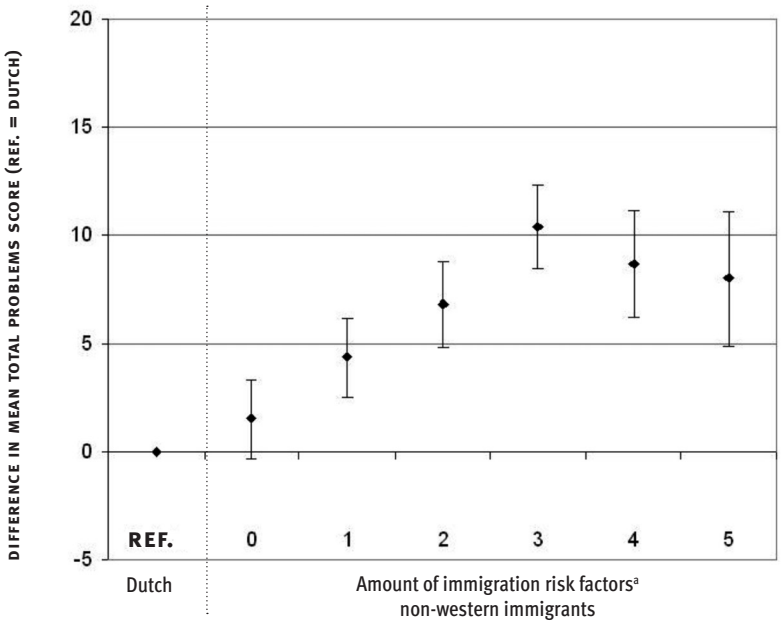


FIGURE 2B. ADJUSTED[b] ASSOCIATION BETWEEN IMMIGRATION RISK INDEX[a] IN NON-WESTERNS AND CBCL TOTAL PROBLEMS



DISCUSSION

This large population-based study in the Netherlands showed that mothers of non-Dutch origin report more behavioural problems in their toddlers as compared to Dutch parents. In contrast with our hypothesis, the higher scores were observed both in children of non-Western origin as in toddlers of non-Dutch European background. The behavioural problems among non-Dutch toddlers were partially explained by family risk factors. In addition, the parent reported behavioural problems of non-Dutch children were more pronounced among those with several unfavourable maternal immigration characteristics.

STRENGTHS AND LIMITATIONS

Before we discuss these findings, some methodological comments have to be made. The strengths of the present study are the large number of participating mother-child dyads from diverse national origins, its population based design, and the use of the age-appropriate and validated CBCL/1½ - 5 to obtain information on child behaviour. However, our research also has some limitations. The non-response analyses indicated that data on the CBCL/1½ - 5 were more complete in children of higher educated and non-single mothers, a trend that was found in Dutch and non-Dutch toddlers. This selective attrition resulted in an under-

representation of both Dutch and non-Dutch children of the most disadvantaged groups, who are at increased risk for behavioural problems. Secondly, our research assistants helped a few participants (all illiterate, mostly Berber Moroccan mothers) filling out the questionnaires. This may have resulted in social desirable answers. A third limitation is that we had to rely on a parent report of children's behavioural problems, as it was not feasible to obtain clinical diagnoses in such a large number of children and the toddlers are too young to be assessed by teachers or other informants. Fourthly, although data was available, it was not possible to adjust the analyses for factors related to religion and beliefs, as the Dutch reference group was nearly exclusively Christian or atheist. Finally, another limitation of our research is the use of several single item measures to assess the association between immigration characteristics and child behavioural problems. Single item measures have psychometric restrictions, such as the tendency to be less reliable than multiple item scales. Although some of the studied immigration characteristics can be measured using multidimensional scales, we used single items for practical reasons. Furthermore, if the construct being measured is sufficiently narrow or is unambiguous to the respondent -which is certainly the case for some of the immigration characteristics-, a single item measure may be adequate.[27]

PARENT REPORTED BEHAVIOURAL PROBLEMS IN IMMIGRANT CHILDREN

The principle finding of the present study, namely more behavioural problems in toddlers of immigrant mothers, compares well with several large studies in school-aged children conducted in the Netherlands and the United States. In these studies, parents of children of different national origins also reported higher levels of child behavioural problems as compared to native parents.[2-6] More specifically, and also in line with our observation, the differences between children of Dutch and non-Dutch origin were more pronounced for internalizing than for externalizing problems in previous Dutch studies,[2 4-6] although reporting bias may explain this finding.[28]

Our results are less congruent with other, mostly smaller, studies on parent reported behavioural problems in school-aged immigrant children, that found no association[7 8] or reported that immigrant children displayed less behavioural problems than native children.[9 10] An explanation that may underlie this discrepancy is the small sample size that leads to reduced power in some of the above studies–e.g. data was available in 106 Greek native and Soviet immigrant children[8] or 200 Gujarati and English native children only[10].The divergence in results may also be related to immigration policies of host countries. For instance, Beiser and colleagues[9] argue that selection mechanisms may explain their study finding: immigrant children had lower levels of behavioural problems than their Canadian-born counterparts due to Canadian immigration policy. Many immigrant households in Canada consist of well-educated, occupationally skilled, healthy people, a selection that does not apply to the Netherlands.

EXPLAINING THE ASSOCIATION BETWEEN NATIONAL ORIGIN AND CHILD BEHAVIOURAL PROBLEMS

The present study demonstrated that among European and non-Western mothers adverse circumstances such as low socioeconomic status, single motherhood, and psychopathological symptoms, are more prevalent than among Dutch mothers. In line with research indicating that such family characteristics are risk factors of behavioural problems in the offspring,[11 12 29] we showed that these factors together explained part of the behavioural problems in toddlers of non-Dutch origin. In some of the immigrant groups the effect of family risk factors was particularly marked. Surinamese toddlers, for instance, displayed hardly more behavioural problems than Dutch children after adjustment for several adverse family circumstances. Maternal education and family income explained a small part of behavioural problems of toddlers of various non-Dutch backgrounds, which is consistent with results of previous studies.[2 4 5] Maternal psychopathology during pregnancy turned out to be an important explanatory variable. This may be due to several mechanisms. First, maternal psychological well being during pregnancy may affect growth and brain development of the fetus. For example, Teixeira and colleagues[30] reported that maternal anxiety during pregnancy was associated with reduced blood flow through the uterine arteries, which affects fetal development. Second, genetic factors may be involved, since twin and adoptee studies indicate a substantial genetic influence on behavioural problems.[31] Third, since maternal mental health during and after pregnancy are highly associated,[32] maternal psychopathology as measured during pregnancy in our study might also affect child behaviour due to the interaction between the mother and her child. Finally, reporter bias is a possible explanation, because a parent report of child behaviour may reflect the well being of the child as well as the well being of the parent.

Maternal psychopathology and other family risk factors play an important role in the behaviour development of toddlers of non-Dutch origin, but these factors did not fully explain the behavioural problems of most immigrant children. Our results also stress the significance of the immigration process, as mothers with several immigration risks reported more behavioural problems in their toddlers than mothers without immigration risks. Whereas several studies among adult and adolescent immigrants indicated that immigration characteristics affect immigrant's mental health,[13 14] little research has examined the effect of parental immigration characteristics on offspring's behavioural problems.[16] Our finding that maternal immigration risks affect offspring's health might be explained in light of the presumptions about acculturation. Acculturation is generally described as the process by which individuals adopt the attitudes, customs, and behaviours of another culture.[33] Often used indexes of acculturation are generational status, length of residence and language use, which are similar to the immigration characteristics we examined.[34] The process of acculturation presents several challenges and life changes that might affect health of immigrants, both beneficially and adversely. Despite growing evidence of an association between acculturation and health, little is known about underlying mechanisms. It has been posited that acculturation

is a proxy for other variables, such as prolonged exposure to stressful events or adverse circumstances associated with immigration (e.g. loss of social networks), settlement in a host country (e.g. discrimination), and disadvantaged social status.[34] In line with this theory, we reason that maternal immigration characteristics as reported during pregnancy influence toddler's behaviour through stress that results from adjustment to a new culture, language difficulties, feelings of rejection, and not feeling at home in a country. Chronic maternal stress in pregnancy may expose the fetus to increased levels of stress hormones.[35] Adaptation of the fetus to this 'stressful' fetal environment possibly influences its development of stress systems. It is also possible that maternal stress associated with the acculturation process affects child behaviour due to the interaction between mother and her child.

There are several potential explanations for the elevated behavioural problem scores that cannot be ascribed to the family risk factors and immigration characteristics in toddlers of non-Dutch origin (i.e. the unexplained variance). Possibly, cultural differences in parent reported behavioural problems are involved. Dissimilar expectancies and beliefs with respect to appropriate child behaviour[36] and differences in threshold to report problems[37] across cultures may lead to perceptual differences between parents of various national origins. In this respect, it should also be considered that the lower scores of Dutch as compared to non- Dutch toddlers might reflect a tendency of Dutch parents to underreport child behavioural problems. This is, however, unlikely, as research comparing the CBCL Total problem score of 31 societies indicated that the mean score of Dutch children was rather average instead of exceptionally low in comparison with other countries.[37] Second, we cannot rule out that genetic factors underlie differences in behaviour problem scores between Dutch and non-Western toddlers. This would imply that the genetic vulnerability for behavioural problems also predisposes to immigration.[31] An alternative interpretation that the genetic background of indigenous Dutch children is particularly protective against behavioural problems as compared to the genetic make-up of other national groups is not very plausible. A third possible explanation for the remaining difference in behavioural problem score between native and non-Western children may be residual effects of immigration characteristics that were not captured by our measures. For instance, we did not consider the effects of racism and discrimination, while this causes high levels of stress and may have far-reaching consequences for immigrants. It has even been reported that discrimination perceived by immigrants seems to contribute to their elevated risk of schizophrenia.[38] Furthermore, we lacked information on traumatic events, whereas research on adolescents indicated that parental experience of traumatic events before and during immigration has a strong effect on mental well-being of the offspring.[39] Moreover, we only studied the effects of immigration characteristics of the mothers, while paternal immigration characteristics might explain an additional part of the behavioural problems of toddlers of non-Western origin.

IMPLICATIONS

Firstly, our research has scientific implications. Future research using other informants is needed to replicate and complement our findings. Since it is known that levels of problem behaviour in adolescents vary with the informant questioned[40], the validity of our results would improve if multiple informants were included. However, information provided by other informants should also be evaluated cautiously. It has, for instance, been reported that teachers scored Asian immigrant children higher on hyperactivity symptoms than native British children, whereas more objective measures of hyperactivity indicated similar prevalence in both groups.[41] Secondly, the differences in behaviour scores between native and immigrant children living in The Netherlands have societal implications, as behavioural problems early in life tend to persist over time and may represent early symptoms of later psychopathology.[17] Our results imply that both researchers and policy makers aiming to tackle ethnic disparities in behavioural problems should take into account the intertwined nature of national origin and family risk factors. Programs should be developed in order to improve family circumstances within the immigrant families. Furthermore, the effect of maternal immigration characteristics on child behavioural problems underlines the importance of acquiring language skills and of feeling accepted by the host culture. This implies that immigrants should, to some extent, adjust to the host country, but it also implies that a host country must give immigrants the *opportunity* to integrate within the society.

REFERENCES

1. Carta MG, Bernal M, Hardoy MC, Haro-Abad JM, Report on the Mental Health in Europe Working Group. Migration and mental health in Europe (the state of the mental health in Europe working group: appendix 1). *Clin Pract Epidemol Ment Health* 2005;1:13.
2. Bengi-Arslan L, Verhulst FC, van der Ende J, Erol N. Understanding childhood (problem) behaviors from a cultural perspective: comparison of problem behaviors and competencies in Turkish immigrant, Turkish and Dutch children. *Soc Psychiatry Psychiatr Epidemiol* 1997;32(8):477-84.
3. Gross D, Fogg L, Young M, Ridge A, Cowell JM, Richardson R, et al. The equivalence of the Child Behavior Checklist/1 1/2-5 across parent race/ethnicity, income level, and language. *Psychol Assess* 2006;18(3):313-23.
4. Stevens GW, Pels T, Bengi-Arslan L, Verhulst FC, Vollebergh WA, Crijnen AA. Parent, teacher and self-reported problem behavior in The Netherlands: comparing Moroccan immigrant with Dutch and with Turkish immigrant children and adolescents. *Soc Psychiatry Psychiatr Epidemiol* 2003;38(10):576-85.
5. Vollebergh WA, ten Have M, Dekovic M, Oosterwegel A, Pels T, Veenstra R, et al. Mental health in immigrant children in the Netherlands. *Soc Psychiatry Psychiatr Epidemiol* 2005;40(6):489-96.
6. Reijneveld SA, Harland P, Brugman E, Verhulst FC, Verloove-Vanhorick SP. Psychosocial problems among immigrant and non-immigrant children–ethnicity plays a role in their occurrence and identification. *Eur Child Adolesc Psychiatry* 2005;14(3):145-52.
7. Alati R, Najman JM, Shuttlewood GJ, Williams GM, Bor W. Changes in mental health status amongst children of migrants to Australia: a longitudinal study. *Soc Health Illness* 2003;25(7):866-888.
8. Kolaitis G, Tsiantis J, Madianos M, Kotsopoulos S. Psychosocial adaptation of immigrant Greek children from the former Soviet Union. *Eur Child Adolesc Psychiatry* 2003;12(2):67-74.
9. Beiser M, Hou F, Hyman I, Tousignant M. Poverty, family process, and the mental health of immigrant children in Canada. *Am J Public Health* 2002;92(2):220-7.
10. Hackett L, Hackett R, Taylor DC. Psychological disturbance and its associations in the children of the Gujarati community. *J Child Psychol Psychiatry* 1991;32(5):851-6.
11. Campbell SB. Behavior problems in preschool children: a review of recent research. *J Child Psychol Psychiatry.* 1995;36(1):113-49.
12. Rutter M, Yule B, Quinton D, Rowlands O, Yule W, Berger M. Attainment and adjustment in two geographical areas: III–Some factors accounting for area differences. *Br J Psychiatry* 1975;126:520-33.
13. Bhugra D. Migration and mental health. *Acta Psychiatr Scand* 2004;109(4):243-58.
14. Lerner Y, Kertes J, Zilber N. Immigrants from the former Soviet Union, 5 years post-immigration to Israel: adaptation and risk factors for psychological distress. *Psychol Med* 2005;35(12):1805-14.
15. Stevens GW, Vollebergh WA, Pels TV, Crijnen AA. Predicting externalizing problems in Moroccan immigrant adolescents in the Netherlands. *Soc Psychiatry Psychiatr Epidemiol* 2005;40(7):571-9.
16. Spencer JH, Le TN. Parent refugee status, immigration stressors, and Southeast Asian youth violence. *J Immigr Minor Health* 2006;8(4):359-68.
17. Carter AS, Briggs-Gowan MJ, Davis NO. Assessment of young children's social-emotional development and psychopathology: recent advances and recommendations for practice. *J Child Psychol Psychiatry* 2004;45(1):109-34.
18. Jaddoe VW, van Duijn CM, van der Heijden AJ, Mackenbach JP, Moll HA, Steegers EA, et al. The Generation R Study: design and cohort update until the age of 4 years. *Eur J Epidemiol* 2008.
19. Statistics Netherlands. Allochtonen in Nederland 2004. Voorburg/Heerlen. 2004b.

20. Achenbach TM, Rescorla LA. *Manual for the ASEBA Preschool Forms & Profiles*. Burlington: University of Vermont, Research Center for Children, Youth & Families, 2001a.
21. Tick NT, van der Ende J, Koot HM, Verhulst FC. 14-year changes in emotional and behavioral problems of very young Dutch children. *J Am Acad Child Adolesc Psychiatry* 2007;46(10):1333-40.
22. Achenbach TM, Becker A, Dopfner M, Heiervang E, Roessner V, Steinhausen HC, et al. Multicultural assessment of child and adolescent psychopathology with ASEBA and SDQ instruments: research findings, applications, and future directions. *J Child Psychol Psychiatry* 2008;49(3):251-275.
23. Vedder P, van de Vijver F. With whom and how we worked. In: Berry J, Phinney J, Sabatier C, Sam D, editors. *Immigrant youth in cultural transition.* Hillsdale, NJ: Erlbaum, 2004.
24. Derogatis LR. *Brief Symptom Inventory (BSI): Administration, scoring and procedures. Manual, third edition*. Minneapolis, MN, USA, 1993.
25. *Standaard Onderwijsindeling 2003, Voorburg/Heerlen.* Statistics Netherlands, 2004a.
26. Rothman KJ, Greenland S. *Modern epidemiology (2nd ed.)*. Philadelphia: Lippincott-Raven Publishers., 1998.
27. Sackett PR, Larson JR. Research Strategies and Tactics in Industrial and Organizational Psychology. In: Dunnette MD, Hough LM, editors. *Handbook of Industrial and Organizational Psychology (2nd ed., vol. 1, pp. 419-489)*. Palo Alto, CA: Consulting Psychologists Press. , 1990.
28. Zwirs BW, Burger H, Buitelaar JK, Schulpen TW. Ethnic differences in parental detection of externalizing disorders. *Eur Child Adolesc Psychiatry* 2006;15(7):418-26.
29. Rutter M, Cox A, Tupling C, Berger M, Yule W. Attainment and adjustment in two geographical areas. I--The prevalence of psychiatric disorder. *Br J Psychiatry* 1975;126:493-509.
30. Teixeira JM, Fisk NM, Glover V. Association between maternal anxiety in pregnancy and increased uterine artery resistance index: cohort based study. *Bmj* 1999;318(7177):153-7.
31. van der Valk JC, Verhulst FC, Stroet TM, Boomsma DI. Quantitative genetic analysis of internalising and externalising problems in a large sample of 3-year-old twins. *Twin Res* 1998;1(1):25-33.
32. Milgrom J, Gemmill AW, Bilszta JL, Hayes B, Barnett B, Brooks J, et al. Antenatal risk factors for postnatal depression: a large prospective study. *J Affect Disord* 2008;108(1-2):147-57.
33. LaFromboise T, Coleman HL, Gerton J. Psychological impact of biculturalism: evidence and theory. *Psychol Bull* 1993;114(3):395-412.
34. Abraido-Lanza AF, Armbrister AN, Florez KR, Aguirre AN. Toward a theory-driven model of acculturation in public health research. *Am J Public Health* 2006;96(8):1342-6.
35. Gitau R, Cameron A, Fisk NM, Glover V. Fetal exposure to maternal cortisol. *Lancet* 1998;352(9129):707-8.
36. Hackett L, Hackett R. Parental ideas of normal and deviant child behaviour. A comparison of two ethnic groups. *Br J Psychiatry* 1993;162:353-7.
37. Rescorla L, Achenbach TM, Ivanova MY, Dumenci L, Almqvist F, Bilenberg N, et al. Behavioural and Emotional Problems Reported by Parents of Children Ages 6 to 16 in 31 Societies. *J Emotional Beh Disorders* 2007;15(3):130-142.
38. Veling W, Selten JP, Susser E, Laan W, Mackenbach JP, Hoek HW. Discrimination and the incidence of psychotic disorders among ethnic minorities in The Netherlands. *Int J Epidemiol* 2007;36(4):761-8.
39. Scharf M. Long-term effects of trauma: psychosocial functioning of the second and third generation of Holocaust survivors. *Dev Psychopathol* 2007;19(2):603-22.
40. Stevens GW, Vollebergh WA. Mental health in migrant children. *J Child Psychol Psychiatry* 2008;49(3):276-294.
41. Sonuga-Barke EJS, Kuldeep M, Taylor EA, Sandberg S. Inter-ethnic bias in teacher's ratings of childhood hyperactivity. *Br J PDevelop Psychol* 1993;11(2):187-200.

CHAPTER **3.3**

Early determinants of maternal and paternal harsh discipline

ABSTRACT

Several studies described risk factors of maternal use of harsh discipline, but knowledge about determinants of paternal harsh discipline is lacking. We examined whether sociodemographic and psychosocial characteristics measured during pregnancy prospectively predict maternal and paternal harsh discipline. Harsh discipline was assessed in the Generation R Study in parents of 3-year-old children using an adapted version of the Parent-Child Conflict Tactics Scale. Data were available for 3756 children and both parents, and for 1100 children and mothers without a participating partner. Non-Western ethnicity, family dysfunction, psychopathology, and a history of delinquency were independently associated with an increased risk of both maternal and paternal harsh discipline. In mothers, indicators of socioeconomic status, such as financial difficulties, educational level and young age were also associated with harsh discipline. Our results suggest that health care workers need to be made aware that mothers *and* fathers with psychosocial problems are at risk of using harsh discipline.

INTRODUCTION

Harsh discipline is characterized by a parent's aim to control a child using verbal violence or physical forms of punishment.[1] Examples are yelling, threatening, and hitting. During the past decades, research has indicated that parental use of harsh discipline presents a risk to healthy child development.[2] More specifically, harsh discipline strategies like shouting and hitting have been linked with aggression, conduct disorder, and other externalizing behavioural problems in the offspring.[2-4] Being spanked during childhood has also been associated with lifetime prevalence of anxiety disorder and alcohol abuse.[2 5] These effects appear to be independent of pre-existing child behavioural problems.[6] Another hazard for children's wellbeing and development associated with harsh discipline is the considerable risk that parental use of harsh discipline strategies results in child maltreatment over time.[7 8]

Given these harmful consequences, it is important to identify determinants of parental use of harsh discipline. Young maternal age, single motherhood, and various indicators of low socioeconomic status have been associated with harsh discipline, although rather inconsistently.[9-16] Studies carried out in the United States repeatedly indicated that African-American mothers more frequently rely on harsh discipline than white-Caucasian mothers.[9 12-18] Additionally, research on the influence of psychosocial characteristics pointed out that mothers who score high on psychopathology and family dysfunction are more likely to use harsh discipline.[10 19-21] Other psychosocial factors such as parental aggressive or violent behaviour and physical abuse during parents' childhood have also been associated with use of harsh discipline by parents themselves.[9 11 12 22] However, not only parental characteristics, but also several child characteristics are related to harsh discipline. For instance, boys appear to face harsh discipline more frequently than girls.[12 13 16] Furthermore, even though harsh discipline seems to cause behavioural problems in the offspring, difficult child behaviour may also provoke the use of harsh discipline by parents.[6]

To date, research primarily focussed on risk factors of *maternal* use of harsh discipline, whereas studies on determinants of *paternal* harsh discipline are very scarce. Likewise, aims to identify paternal determinants of physical child abuse have also started only recently.[23-25] Furthermore, previous etiologic studies often relied on cross sectional designs or assessed determinants of harsh discipline when the child was already a few years old.[9-17 19-21] This makes it difficult to infer about direction of effects between characteristics under study and harsh discipline, as it has been suggested that child behaviour influences both parenting styles and even parental characteristics, such as family stress.[26]

The aim of the present study is to examine sociodemographic and psychosocial determinants of both maternal and paternal use of harsh discipline. For this, we used data from a large cohort in the Netherlands. In order to study determinants of harsh discipline independently of child behaviour, we assessed all parental determinants before birth of the child. This will also enable us to establish to what extent families at risk for harsh discipline can be identified during pregnancy. We

hypothesize that the determinants of paternal use of harsh discipline are similar to those that have been identified as determinants of maternal harsh discipline.

METHODS

DESIGN AND STUDY POPULATION

This study was embedded in Generation R, a population-based cohort from fetal life onwards.[27 28] Briefly, pregnant women living in the study area in Rotterdam, the Netherlands, with an expected delivery date between April 2002 and January 2006 were invited to participate. Written informed consent was obtained from all participants. The Medical Ethical Committee of the Erasmus Medical Centre, Rotterdam, has approved the study.

Full consent for the postnatal phase of the Generation R Study was obtained from 7295 children. Children without information on maternal harsh discipline (n = 2439) were excluded, yielding a sample size of 4856 mother-child dyads for the present study. The response rate for the questionnaire on maternal discipline was 67% (4856/7295). Data on paternal harsh discipline was available for 3756 of these mother-child dyads. This selection in available data on paternal harsh discipline was partly due to single motherhood: 22% (n = 242) of the 1100 mothers without a participating partner actually had no partner. We conducted the analyses both in the group of 4856 mothers and the group of 3756 parents to make results of mothers and fathers comparable.

HARSH DISCIPLINE

Use of harsh discipline of both parents was assessed with an adapted version of the Parent-Child Conflict Tactics Scale (CTS-PC) when the children were 3 years old.[29] This instrument was designed to obtain self-reported ratings of use of various discipline types by parents. We included three subscales of the CTS-PC in our assessment, namely Non-Violent Discipline, Psychological Aggression and Physical Assault. To make the assessed scales age-appropriate for our study population of 3-year-old children, we excluded one item of the Psychological Aggression scale and three items of Physical Assault (e.g. 'Said you would send child away or kick hem/her out of the house'). The present study regards only the Psychological Aggression and Physical Assault scales and does not include Non-Violent Discipline. We combined the six items of the Psychological Aggression and Physical Assault scales into one scale, which we labelled 'harsh discipline' (see items in Table 2). Cronbach's alphas for the harsh discipline scale were α = .63 for the mothers and α = .57 for the fathers, indicating reasonable internal consistency. Parents rated the occurrence of harsh discipline (6 items) during the past two weeks on a 6-point scale ranging from 'never' to 'five times or more'. Due to very low prevalence rates, we combined the categories 'twice', 'three times', 'four times' and 'five times'. This resulted in three categories: 'never' (0), 'once' (1) and 'twice or more' (2). The harsh discipline sumscore was calculated by adding the six items. This

yielded a score ranging from 0 to 12 (mothers: $M = 2.2$, $SD = 1.97$; fathers: $M = 1.8$, $SD = 1.82$), with higher scores reflecting higher incidence of harsh discipline.

DETERMINANTS

Information on the determinants was obtained by questionnaire during pregnancy. Mothers and fathers filled out separate questionnaires to report on their own characteristics. Based on the literature,[9-17 19-21] we considered the following sociodemographic and psychosocial characteristics as possible determinants of harsh discipline.

Parental *educational level* was defined by the highest attained educational level and divided in four categories ranging from 'high' to 'low' according to the definition of Statistics Netherlands.[30] *Ethnicity* was based on country of birth of the parents of the parent. In accordance with Statistics Netherlands,[31] we classified a mother or father as non-Dutch if one of her/his parents was born abroad. The non-Dutch parents were differentiated into non-Dutch European and non-Western origins. Those with a non-Western background were further subdivided into first and second generation immigrants. For ease of interpretation, parental age was categorized as <25 years, 25-35 years, and >35 years. A *history of delinquency* was assessed by 18 items regarding different types of delinquent behaviour, such as travelling in public transport without paying, stealing, demolishing other persons' belongings or giving a wrong declaration to an insurance company.[32] We categorized self-reported delinquency as follows: no history of delinquency, petty crimes, and history of more serious crimes. Furthermore, parents were asked to fill out whether they had *ever been addicted* to any substance or activity, such as alcohol, medication, drugs or gambling (yes or no). Smoking was not categorized as an addiction. Symptoms of *psychopathology* were assessed using the Brief Symptom Inventory (BSI), a validated self-report.[33] The weighted sumscore of the 53 items indicates the global severity of psychopathology. We also calculated specific symptom scales of *hostility* (5 items) and *depression* (6 items). *Family functioning* as perceived by the parent was measured with the General Functioning scale of the McMasters Family Assessment Device (FAD).[34] In this validated self-report questionnaire, parents were asked to rate family functioning and family stress on a 4-point scale. The total score is a weighted sum of the 12 items. To allow descriptive comparison between mothers and fathers, and to facilitate interpretation of the findings, the sumscores of the FAD and BSI were dichotomized: those in the highest 20% of the scales were categorized as high-scorers indicating high levels of family dysfunction or psychopathology.

Mothers reported on family income and financial difficulties. These variables were also examined as determinants of paternal harsh discipline. *Family income* was defined by the total net month income of the household and dichotomized into '<2000 euros' and '>2000 euros'. Additionally, mothers answered the question whether the family experienced *financial difficulties* (yes or no). Finally, mothers were asked to report their *marital status*, which was categorized as 'married or cohabiting' and 'single'. Mothers were also asked to filled out the 34-item short version of the *Childhood Trauma Questionnaire* (CTQ), a retrospective self-report measure of the

frequency and severity of neglect and abuse in childhood and adolescence.[35] Of the CTQ, the *Physical Abuse scale* (5 items) is used in the present study. The sumscore was dichotomized: the 20% highest scoring mothers were categorized as having experienced physical abuse during childhood. The CTQ was not completed by fathers.

Information on *child gender* was obtained from the medical records completed by community midwives and obstetricians.

STATISTICAL ANALYSES

All analyses were performed using the Statistical Package of Social Sciences version 11.0 for Windows (SPSS Inc, Chicago, IL, USA). We compared the prevalence of the different items of harsh discipline between mothers and fathers with the Wilcoxon signed-ranks test for non-parametric paired observations, which yields a *Z*-statistic. We dichotomized the harsh discipline sumscores for the regression analyses, because the distribution was skewed due to a very small number of frequent harsh discipline users. As there is no standard cutoff point for the CTS-PC,[29] we considered the 20% highest scoring mothers and fathers as parents who use harsh discipline. Univariate logistic regression analyses were performed to calculate odds ratios (ORs) for maternal and paternal use of harsh discipline as compared to non-users. We tested for two-way interactions between gender, ethnicity and educational level. Next, multivariate logistic regression analyses were performed to calculate adjusted ORs; only variables that were significantly associated with harsh discipline in the univariate analyses ($p<.05$) were included in the multivariate model. Missing values of the determinants were replaced by the median, if less than 10% of the data was missing. A category 'missing' was added to variables with more than 10% missing values, which were: ever been addicted, delinquency history, BSI-scales, FAD, and CTQ. The ORs for the missing categories are not presented in the tables. The association between marital status and harsh discipline was only calculated in the total group of 4856 mothers, as the percentage of single mothers in the subgroup of mothers *with* a participating father ($n=3756$) was rather small (3%).

NON-RESPONSE ANALYSIS

Mothers with missing data on harsh discipline (n=2439) were compared with mothers who filled out the questions on harsh discipline (n=4856). Data on maternal harsh discipline was more often missing in mothers who were first or second generation non-Western immigrant ($\chi^2(3, 7295) = 394$, $p<.001$), lower educated ($\chi^2(3, 7295) = 390$, $p<.001$), single parent ($\chi^2(1, 7295) = 162$, $p<.001$), and younger than 25 ($\chi^2(2, 7295) = 418$, $p<.001$) as compared to mothers who filled out the questions on harsh discipline.

TABLE 1. CHARACTERISTICS OF THE STUDY POPULATION (n=3756)

DETERMINANTS	MOTHERS	FATHERS
Gender child (% boy)	49.5	
Sociodemographic characteristics of families		
Family income (% <2000 euros)	19.1	
Financial difficulties (% yes)	12.0	
Sociodemographic characteristics of mothers / fathers		
Age: >35 years (%)	21.1	36.5
25-35 years (%)	74.2	61.8
<25 years (%)	4.7	1.6
Ethnicity: Dutch (%)	72.1	74.7
Other European (%)	8.7	6.1
Non-Western, 1st generation (%)	11.1	8.2
Non-Western, 2nd generation (%)	8.1	11.0
Educational level: High (%)	37.0	40.4
Mid-high (%)	26.8	22.1
Mid-low (%)	26.1	24.5
Low (%)	10.1	13.1
Psychosocial characteristics of mothers / fathers		
Delinquency history: No delinquency (% yes)	59.3	38.7
Petty crime (% yes)	17.0	11.8
Serious crime (% yes)	23.7	49.5
Ever been addicted (% yes)	2.1	8.3
Global psychopathology score (high)[$]	18.4 (0.33)	20.6 (0.19)
Hostility score (high)[$]	24.6 (0.26)	39.7 (0.10)
Depression score (high)[$]	29.6 (0.01)	20.0 (0.01)
Perceived family dysfunction (high)[¶]	18.0 (1.92)	21.3 (1.83)
Physically abused by parents (yes)[£]	13.9 (6.00)	No information

Values are percentages; scores between parentheses indicate the cut off scores for the 20% highest scores.
[$] Measured with the Brief Symptom Inventory.
[¶] Measured with the Family Assessment Device.
[£] Measured with the Childhood Trauma Questionnaire.

RESULTS

Characteristics of the study population are presented in TABLE 1. 49.5% of the children were boys and 50.5% girls. 27.9% of the mothers and 25.3% of the fathers were of non-Dutch ethnicity.

The prevalence of the various harsh discipline items is presented in TABLE 2. The prevalence of shouting was particularly high: 76.8% of the mothers and 67.3% of the fathers reported to have shouted angrily at their child at least once during the past two weeks. Compared to fathers, mothers more often shouted (Z=-11.7, p<.001) or threatened to slap (Z=-6.0, p<.001). Fathers more often called their child dumb or lazy than mothers did (Z=-3.1, p=.002). There were no significant differences between mothers and fathers in prevalence of scolding, shaking, or pinching the child's arm.

Next, we compared mothers with (n=3756) and without (n = 1100) data available on their partner's use of harsh discipline. The latter group of mothers was more often of non-Western origin ($\chi^2(3, 4856) = 446$, p<.001), lower educated ($\chi^2(3, 4856) = 325$, p<.001), single parent ($\chi^2(1, 4856) = 405$, p<.001), and younger than 25 ($\chi^2(2, 4856) = 139$, p<.001).

In TABLE 3 the univariate associations between determinants and harsh discipline are presented for the total group of mothers (n=4856) and for the mothers with participating fathers (n=3756). Whereas the first is more representative, the second can be compared to fathers straightforwardly. The magnitude of the ORs for harsh discipline and the levels of statistical significance are fairly similar in both groups of mothers. Experiencing financial difficulties is a typical example of the determinants of harsh discipline: the OR of financial difficulties was 2.13 (95% CI: 1.79, 2.53) in the total group of 4856 mothers, very similar to the OR of 2.08 (95% CI: 1.66, 2.61) in the subgroup of 3756 mothers. The similarity indicates that the results are not distorted by selective participation of fathers.

TABLE 2. PREVALENCE OF HARSH DISCIPLINE (n = 3756)

		PREVALENCE IN PAST TWO WEEKS (%)			COMPARING PERCENTAGES MOTHER AND FATHER	
HARSH DISCIPLINE ITEMS	PARENT	NEVER[$]	ONCE[$]	TWICE OR MORE[$]	Z-TEST STATISTIC[¶]	P-VALUE
I shouted, yelled or screamed angrily at my child	Mother	23.2	28.5	48.3	-11.66	‹0.001
	Father	32.7	28.8	38.5		
I scolded at my child	Mother	95.4	2.5	2.1	-1.50	0.135
	Father	95.8	2.6	1.6		
I threatened to slap, spank or hit my child but did not actually do it	Mother	74.5	12.4	13.1	-5.95	‹0.001
	Father	79.1	10.6	10.2		
I called my child dumb or lazy or some other name like that	Mother	94.5	3.3	2.2	-3.06	0.002
	Father	93.0	4.1	2.9		
I shook my child	Mother	94.4	3.8	1.8	-0.20	0.840
	Father	94.3	4.1	1.6		
I angrily pinched my child in his/her arm	Mother	84.9	9.9	5.2	-0.58	0.561
	Father	84.3	10.5	5.1		
		Median harsh discipline score (100% range)[£]				
	Mother	2.00 (0-12.00)				
	Father	1.00 (0-12.00)				

[$] Values are percentages.
[¶] Calculated with Wilcoxon signed-ranks test for non-parametric paired observations.
[£] Calculated by summing the individual items (never=0, once=1, twice or more=2).

TABLE 3. UNIVARIATE ASSOCIATIONS BETWEEN DETERMINANTS AND *maternal* HARSH DISCIPLINE

	OR FOR HIGH LEVELS OF HARSH DISCIPLINE (95% CI)[¶]	
DETERMINANTS	**ALL MOTHERS (*n*=4856)**	**MOTHERS WITH PARTICIPATING FATHER (*n*=3756)**
Gender child (boy)	1.25 (1.09, 1.44) **	1.37 (1.16, 1.61) ***
Sociodemographic characteristics of families		
Family income (low)	2.00 (1.72, 2.31) ***	1.74 (1.43, 2.11) ***
Financial difficulties (yes)	2.13 (1.79, 2.53) ***	2.08 (1.66, 2.61) ***
Sociodemographic characteristics of mothers		
Age: 25-35 years (vs. >35 years)	1.26 (1.05, 1.51) *	1.31 (1.06, 1.63) *
<25 years (vs. >35 years)	2.80 (2.13, 3.69) ***	2.86 (1.98, 4.13) ***
Ethnicity: Other European (vs. Dutch)	1.86 (1.46, 2.38) ***	2.14 (1.64, 2.79) ***
Non-Western, 1st generation (vs. Dutch)	2.74 (2.30, 3.25) ***	2.50 (1.97, 3.16) ***
Non-Western, 2nd generation (vs. Dutch)	1.93 (1.52, 2.43) ***	1.79 (1.35, 2.39) ***
Educational level: Mid-high (vs. high)	1.22 (1.01, 1.49) *	1.17 (0.94, 1.46)
Mid-low (vs. high)	1.63 (1.36, 1.96) ***	1.57 (1.27, 1.94) ***
Low (vs. high)	2.33 (1.90, 2.87) ***	2.17 (1.66, 2.85) ***
Marital status (single)	1.95 (1.55, 2.45) ***	Not applicable
Psychosocial characteristics of mothers		
Delinquency history: Petty crime (vs. no history)	1.51 (1.22, 1.86) ***	1.48 (1.16, 1.89) **
Serious crime (vs. no history)	1.68 (1.39, 2.02) ***	1.43 (1.15, 1.78) **
Ever been addicted (yes)	1.17 (0.71, 1.94)	1.14 (0.62, 2.16)
Global psychopathology score (high)	2.04 (1.73, 2.42) ***	1.89 (1.54, 2.33) ***
Hostility score (high)	2.04 (1.72, 2.41) ***	1.76 (1.44, 2.16) ***
Depression score (high)	1.86 (1.58, 2.19) ***	1.82 (1.50, 2.21) ***
Perceived family dysfunction (high)	1.82 (1.52, 2.19) ***	1.76 (1.41, 2.20) ***
Physically abused by parents (yes)	1.89 (1.55, 2.31) ***	1.73 (1.36, 2.21) ***

[¶] Reference is low levels of harsh discipline within the specific subgroup (i.e. all mothers or mother of whom the partner (father of the child) participates).
** p < .05, ** p < .01, *** p < .001.*

TABLE 4 shows the univariate association of sociodemographic and psychosocial characteristics with risk of paternal harsh discipline. As indicated in TABLE 3 (mothers, right column) and TABLE 4 (fathers), younger parents used harsh discipline more often than older parents ($OR_{mothers}$ <25 years = 2.86, 95% CI: 1.98, 4.13; $OR_{fathers}$ <25 years = 1.75, 95% CI: 1.02, 2.99). Furthermore, male gender of the child, being non-Western first generation immigrant, a history of delinquent behaviour, self reported psychopathology and family dysfunction during pregnancy were each associated with higher levels of maternal and paternal harsh discipline (see TABLES 3 and 4). The global psychopathology score predicted harsh discipline similarly as the hostility and depression subscales did (see TABLES 3 and 4). Low family income, having financial difficulties, non-Dutch European or second generation non-Western background, and low educational level were only associated with *maternal* harsh discipline (see TABLES 3 and 4). Finally, a mother's history of physical abuse during her own childhood (OR = 1.73, 95% CI: 1.36, 2.21) was also predictive of harsh discipline; this determinant was not assessed in fathers. History of addiction was not related with maternal or paternal harsh discipline. We found no

significant interaction effects in our data (data not shown).

TABLE 5 shows the fully adjusted risks for harsh discipline. In both mothers and fathers, male gender of the child, non-Western ethnicity (in fathers only first generation immigrant), family dysfunction, psychopathology, and a history of delinquent behaviour remained significant risk factors for harsh discipline, even though the ORs were slightly attenuated in the multivariate model. Financial difficulties, educational level and age were independently associated with maternal, but not with paternal harsh discipline (see TABLE 5). The percentage explained variance in the multivariate models was 8% for the mothers and 4% in the fathers. The percentage explained variance solely by the sociodemographic variables (family income, financial difficulties, age, ethnicity and educational level) was 5% for the mothers and 0.5% for the fathers.

TABLE 4. UNIVARIATE ASSOCIATIONS BETWEEN DETERMINANTS AND *paternal* HARSH DISCIPLINE (n=3756)

DETERMINANTS	OR FOR HIGH LEVELS OF HARSH DISCIPLINE (95% CI)[¶]
Gender child (boy)	1.64 (1.41, 1.90) ***
Sociodemographic characteristics of families	
Family income (low)[#]	1.06 (0.88, 1.28)
Financial difficulties (yes) [#]	0.98 (0.78, 1.23)
Sociodemographic characteristics of fathers	
Age: 25-35 years (vs. >35 years)	1.15 (0.98, 1.34)
<25 years (vs. >35 years)	1.75 (1.02, 2.99) *
Ethnicity: Other European (vs. Dutch)	0.96 (0.70, 1.33)
Non-Western, 1st generation (vs. Dutch)	1.70 (1.31, 2.19) ***
Non-Western, 2nd generation (vs. Dutch)	1.01 (0.79, 1.29)
Educational level: Mid-high (vs. high)	1.07 (0.88, 1.30)
Mid-low (vs. high)	1.05 (0.87, 1.26)
Low (vs. high)	1.06 (0.84, 1.34)
Psychosocial characteristics of fathers	
Delinquency history: Petty crime (vs. no history)	1.47 (1.09, 1.98) *
Serious crime (vs. no history)	1.49 (1.22, 1.82) ***
Ever been addicted (yes)	0.97 (0.69, 1.36)
Global psychopathology score (high)	1.69 (1.38, 2.07) ***
Hostility score (high)	1.66 (1.40, 1.98) ***
Depression score (high)	1.67 (1.36, 2.05) ***
Perceived family dysfunction (high)	1.50 (1.22, 1.83) ***

[¶] Reference is low levels of harsh discipline.
[#] Reported by mothers.
** $p < .05$, ** $p < .01$, *** $p < .001$.*

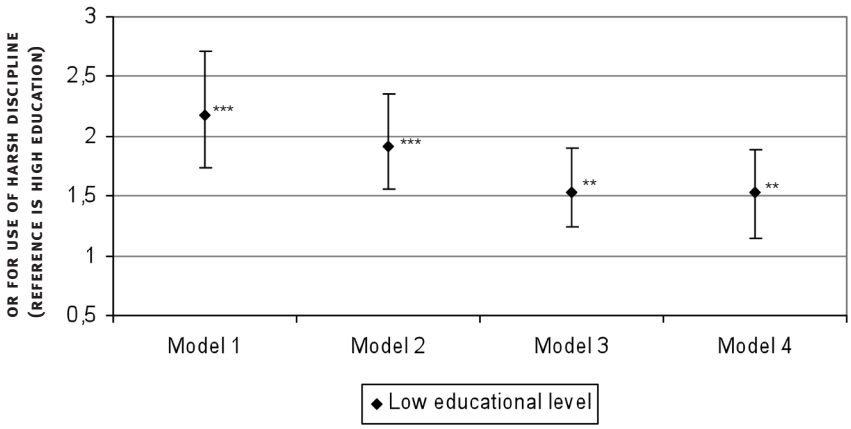
TABLE 5. MULTIVARIATE ASSOCIATIONS BETWEEN DETERMINANTS AND HARSH DISCIPLINE (n=3756)[$]

	OR FOR HIGH LEVELS OF HARSH DISCIPLINE (95% CI)[¶]	
DETERMINANTS	**MOTHERS**	**FATHERS**
Gender child (boy)	1.41 (1.19, 1.67) ***	1.64 (1.41, 1.90) ***
Sociodemographic characteristics of families		
Family income (low) [#]	0.96 (0.75, 1.22)	0.93 (0.75, 1.16)
Financial difficulties (yes) [#]	1.43 (1.10, 1.85) **	0.87 (0.68, 1.13)
Sociodemographic characteristics of mothers / fathers		
Age: 25-35 years (vs. ›35 years)	1.32 (1.06, 1.65) *	1.13 (0.97, 1.32)
‹25 years (vs. ›35 years)	1.74 (1.16, 2.61) **	1.60 (0.91, 2.82)
Ethnicity: Other European (vs. Dutch)	2.13 (1.61, 2.80) ***	0.96 (0.69, 1.33)
Non-Western, 1st generation (vs. Dutch)	1.88 (1.44, 2.45) ***	1.76 (1.33, 2.33) ***
Non-Western, 2nd generation (vs. Dutch)	1.45 (1.07, 1.97) *	1.00 (0.78, 1.30)
Educational level: Mid-high (vs. high)	1.15 (0.92, 1.44)	1.03 (0.85, 1.26)
Mid-low (vs. high)	1.34 (1.06, 1.68) *	0.94 (0.77, 1.15)
Low (vs. high)	1.57 (1.16, 2.13) **	0.95 (0.74, 1.23)
Psychosocial characteristics of mothers / fathers		
Delinquency history: Petty crime (vs. no history)	1.43 (1.11, 1.84) **	1.47 (1.08, 2.00) *
Serious crime (vs. no history)	1.38 (1.10, 1.73) **	1.46 (1.19, 1.79) ***
Global psychopathology score (high)	1.45 (1.14, 1.84) **	1.51 (1.23, 1.87) ***
Hostility score (high) [£]	1.29 (1.04, 1.61) *	1.53 (1.28, 1.84) ***
Depression score (high) [£]	1.39 (1.13, 1.71) **	1.52 (1.23, 1.88) ***
Perceived family dysfunction (high)	1.27 (1.01, 1.62) *	1.34 (1.09, 1.66) **
Physically abused by parents (yes)	1.27 (0.98, 1.65)	No information
Explained variance	8%	4%

[$] All variables presented in the table were included in the model.
[¶] References are low levels of harsh discipline within the specific subgroup (i.e. mothers or fathers).
[#] Reported by mothers.
[£] Multivariate model repeated including this scale instead of the overall psychopathological symptoms score.
** $p < .05$, ** $p < .01$, *** $p < .001$.*

To unravel the mechanisms underlying the association between educational level, as an indicator of socioeconomic status, and maternal harsh discipline ($OR_{\text{low vs high education}}$=2.17, 95% CI: 1.66, 2.85), we performed further analyses comparing the lowest and highest educational levels (FIGURE 1). Stepwise adjustment showed that the association between educational level and maternal harsh discipline was partly confounded by gender and ethnicity (model 2 in FIGURE 1: $OR_{\text{low vs high education}}$=1.91, 95% CI: 1.44, 2.53). Further adjustment indicates that the effect of educational level on harsh discipline is mediated by sociodemographic variables, such as family income and maternal age (model 3 in FIGURE 1: $OR_{\text{low vs high education}}$=1.53, 95% CI: 1.13, 2.07). Once adjusted for confounders and sociodemographic variables, psychosocial determinants did not further mediate the association between educational level and harsh discipline (model 4 in FIGURE 1: $OR_{\text{low vs high education}}$=1.53, 95% CI: 1.12, 2.08).

FIGURE 1. STEPWISE ADJUSTMENT OF THE ASSOCIATION BETWEEN EDUCATIONAL LEVEL (LOW VERSUS HIGH EDUCATIONAL LEVEL) AND MATERNAL HARSH DISCIPLINE (N=3756)



Model 1: unadjusted.
Model 2: model adjusted for gender and ethnicity.
Model 3: model 2 additionally adjusted for sociodemographic characteristics (family income, financial difficulties, maternal age).
Model 4: model 3 additionally adjusted for psychosocial functioning (delinquency history, global psychopathology score, family dysfunction, history of physical abuse).
** p < .05, ** p < .01, *** p < .001.*

DISCUSSION

This large population-based study showed that psychosocial characteristics of parents, such as psychopathology, delinquent behaviour and family dysfunction, predicted the use of harsh discipline by mothers and by fathers. Moreover, being first generation, non-Western immigrant consistently predicted harsh discipline of both parents. Indicators of socioeconomic status, however, were clearly associated with maternal harsh discipline, but hardly predicted paternal use of harsh discipline.

STRENGTHS AND LIMITATIONS

Before discussing these findings in more detail, some methodological comments have to be made. The strengths of the present study are the assessment of both maternal and paternal harsh discipline and the measurement of potential determinants during pregnancy. Other strengths are the large number of participants and the population based design. One of the limitations of our research is that the non-response analyses indicated that data on maternal harsh discipline was more complete in higher educated, non-single, and Dutch mothers. This resulted in an under-representation of the most disadvantaged families, which reduced our power and may have affected our results if the relation between determinants and harsh discipline differed between responding and non-responding mothers. On

the other hand, we showed that the selective participation of fathers did not influence the associations between determinants and maternal harsh discipline. This suggests that the effect of non-response in mothers might also be rather small. Secondly, this study was limited by the use of an adapted version of the CTS-PC to assess harsh discipline. The adaptation was necessary to obtain an age-appropriate instrument for our study population of 3-year-old children. A further modification was the merging of two original scales with several items of harsh discipline into one 'harsh discipline' scale. However, the internal consistencies of the harsh discipline scales of both mothers and fathers indicated a reasonable factor structure, and were similar to the internal consistencies of the original CTS-PC scales.[29] Thirdly, our study assessed harsh discipline by means of a parent-report. Response biases such as social desirability might have affected our data to an unknown degree. Yet, the World Health Organization has recommended self report measures of harsh discipline in population-based studies, because they can yield useful information for prevention policies.[36]

DETERMINANTS OF USE OF HARSH DISCIPLINE

Our research indicated that parents regularly discipline their 3-year-old children by shouting, pinching in the arm or threatening to spank. Several characteristics of parents during pregnancy are associated with harsh discipline later during childhood. Of the included sociodemographic characteristics, non-Western ethnicity independently predicted both maternal and paternal use of harsh discipline. The finding that non-Western parents use harsh discipline more frequently than Dutch parents may be due to several mechanisms. Firstly, ideas about the effects and effectiveness of harsh discipline as well as general beliefs about parenting styles differ between cultural groups. For instance, in some cultures, physical punishment of children is more accepted than in other societies,[37] leading to cultural or ethnic differences in use of harsh discipline. It is important to further investigate the role of these cultural differences in Europe, especially since a few studies in the U.S.A. indicated that the longterm effects of harsh discipline are culture-specific.[38 39] A second explanation for the association between ethnicity and harsh discipline might be that the use of harsh discipline is a taboo in the Netherlands.[40] If Dutch parents are more aware of this than non-Dutch parents, social desirability may have influenced the reports of Dutch parents to a larger extent than reports of parents of other national origins. Finally, non-Dutch parents often live in disadvantaged neighbourhoods and might experience discrimination or integration problems which cause stress. These elevated levels of stress could result in more frequent use of harsh discipline among ethnic minority groups. Among fathers of non-Western background, only being a first generation immigrant was a risk factor for harsh discipline, while second generation immigrants reported similar levels of use of harsh discipline as Dutch fathers. It might be that second generation immigrants experience less stress or are more accustomed to Dutch norms than first generation immigrants and thus use less harsh discipline.

Besides the sociodemographic characteristics, several psychosocial risk factors were also predictive of both maternal and paternal use of harsh discipline. We found that psychopathology, family dysfunction, and a history of delinquent behaviour as measured during pregnancy were associated with parental harsh discipline later during childhood. Previously, explanations have been put forward for the association between psychosocial problems and maternal harsh discipline.[41 42] These explanations might also apply to fathers. Negative parental emotions and tensions are carried over into parent-child interactions, a concept that Almeida and colleagues labelled the 'spillover effect'.[41] Moreover, parents with psychosocial problems may also have little patience or are less able to manage difficult child-rearing situations, resulting in harsh discipline that, at least at the short term, seems to be effective. On the other hand, it is also conceivable that psychosocial dysfunction of parents and harsh discipline are not causally related, but are explained by underlying concepts such as poor interpersonal cognitions or skills.[42]

We hypothesized that substance abuse, also considered as a psychosocial risk factor, would be associated with harsh discipline, as it is an indication of psychopathology and of having poor coping strategies. However, parental history of addiction was not associated with use of harsh discipline, which is in contrast with prior studies.[10 19] The absence of an association may be due to the small number of parents in our study that reported to have been addicted.

The associations between determinants and use of harsh discipline were fairly similar in both mothers and fathers, except for some determinants. We found that indicators of socioeconomic status, like financial difficulties and low educational level, strongly predicted maternal harsh discipline, whereas these indicators were hardly related to paternal harsh discipline. The relation between educational level and maternal harsh discipline was partly explained by other sociodemographic risk factors, but was not fully due to other determinants included in the multivariate model. A possible clarification for the association between indicators of socioeconomic status and harsh discipline is that socioeconomic status reflects general knowledge, literacy, and problem-solving skills,[43 44] which might influence the choice of whether or not to use harsh discipline. One would expect, though, that this does not only pertain to mothers, but also to fathers. In general, however, mothers spend more time with their offspring than fathers, as they are more often primary caregivers.[45] This difference between mothers and fathers might be larger in women of low socioeconomic background as compared to women of high socioeconomic status,[46] while time spent with the child is probably correlated with the number of times a parent has to discipline the child. On the other hand, the lack of an association might also be due to our assessment of indicators of socioeconomic status: family income and financial difficulties were one of the few factors only reported by mothers and not by fathers. As a report on financial difficulties is rather subjective, it is conceivable that only fathers' own experiences of financial concerns is associated with the use of harsh discipline.

We assessed the parental determinants before birth, hence the results were not influenced by child temperament and development. However, it is still possible that the associations between parental determinants and harsh discipline are mediated by child behaviour. For instance, the association between social disadvantage, as indicated by ethnic minority status or low socio-economic position, and child behavioural problems is well established.[47 48] As level of social disadvantage is rather stable, it is probable that social disadvantage (as measured during pregnancy) elicits child behavioural problems, which in turn causes higher levels of harsh discipline.

The only child characteristic examined in this study was gender of the child. We showed that both mothers and fathers discipline boys more often in a harsh way than girls. This might be explained by gender role expectations or experiences. For instance, it has been suggested that parents believe that boys are more aggressive than girls and therefore require more discipline.[13 16] Alternatively, it also conceivable that boys show more rule breaking behaviour and are less compliant, which leads to more frequent use of harsh discipline.[16]

IMPLICATIONS

Due to the harmful consequences of harsh discipline and the link between harsh discipline and child maltreatment, the prevention of it is a major public health goal.[36] Our study indicated that several 3-year-old children were disciplined in a harsh way and that characteristics of both mothers and fathers during pregnancy are predictive of harsh discipline during childhood. The combination of our outcomes and previous research conducted in North America[9-13 15 18] suggests that determinants of maternal harsh discipline are fairly similar across Western societies. Likewise, the psychosocial determinants of harsh discipline are similar for fathers and mothers. As research on determinants of paternal harsh discipline is lacking,[49] it is important that our findings are replicated in future studies.

Some determinants of harsh discipline, like ethnicity, may not be easily amendable, although it is promising to see that second-generation immigrant fathers seem to be less likely to use harsh discipline than first-generation immigrants. Other identified determinants such as parental psychopathology or stressful family circumstances are modifiable.[50 51] Another way to prevent the use of harsh discipline is by educating parents about alternative strategies to discipline their children and by informing them about the consequences of harsh discipline.[52] Preventive interventions should ideally be applied early in children's lives and must have a special focus on socially disadvantaged families and on parents with psychopathology or family stress. Health care workers need to be made aware that both mothers and fathers who experience psychosocial problems are at risk of using harsh discipline.

REFERENCES

1. Chang L, Schwartz D, Dodge KA, McBride-Chang C. Harsh parenting in relation to child emotion regulation and aggression. *J Fam Psychol* 2003;17(4):598-606.
2. Gershoff ET. Corporal punishment by parents and associated child behaviors and experiences: a meta-analytic and theoretical review. *Psychol Bull* 2002;128(4):539-79.
3. McLoyd VC, Smith J. Physical discipline and behavior problems in African American, European American, and Hispanic children: emotional support as moderator. *J Marriage Family* 2002;64:40-53.
4. Vostanis P, Graves A, Meltzer H, Goodman R, Jenkins R, Brugha T. Relationship between parental psychopathology, parenting strategies and child mental health–findings from the GB national study. *Soc Psychiatry Psychiatr Epidemiol* 2006;41(7):509-14.
5. MacMillan HL, Boyle MH, Wong MY, Duku EK, Fleming JE, Walsh CA. Slapping and spanking in childhood and its association with lifetime prevalence of psychiatric disorders in a general population sample. *Cmaj* 1999;161(7):805-9.
6. Larzelere RE. Child outcomes of nonabusive and customary physical punishment by parents: an updated literature review. *Clin Child Fam Psychol Rev* 2000;3(4):199-221.
7. Carey TA. Spare the rod and spoil the child. Is this a sensible justification for the use of punishment in child rearing? *Child Abuse Negl* 1994;18(12):1005-10.
8. Fontes LA. *Child abuse and culture. Working with diverse families.* . New York: Guilford Publications, 2005.
9. Barkin S, Scheindlin B, Ip EH, Richardson I, Finch S. Determinants of parental discipline practices: a national sample from primary care practices. *Clin Pediatr (Phila)* 2007;46(1):64-9.
10. Frias-Armenta M, McCloskey LA. Determinants of harsh parenting in Mexico. *J Abnorm Child Psychol* 1998;26(2):129-39.
11. Simons RL, Whitbeck LB, Conger RD, Chyi-In W. Intergenerational transmission of harsh parenting. *Dev Psychol* 1991;27(1):159-171.
12. Dietz TL. Disciplining children: characteristics associated with the use of corporal punishment. *Child Abuse Negl* 2000;24(12):1529-42.
13. Giles-Sims J, Straus MA, Sugarman DB. Child, maternal, and family characteristics associated with spanking. *Family relations* 1995;44(2):170-176.
14. Gutman LM, Eccles JS. Financial strain, parenting behaviors, and adolescents' achievement: testing model equivalence between African American and European American single- and two-parent families. *Child Dev* 1999;70(6):1464-76.
15. Regalado M, Sareen H, Inkelas M, Wissow LS, Halfon N. Parents' discipline of young children: results from the National Survey of Early Childhood Health. *Pediatrics* 2004;113(6 Suppl):1952-8.
16. Straus MA, Stewart JH. Corporal punishment by American parents: national data on prevalence, chronicity, severity, and duration, in relation to child and family characteristics. *Clin Child Fam Psychol Rev* 1999;2(2):55-70.
17. Weis R, Toolis EE. Parenting across cultural contexts in the USA: assessing parenting behaviour in an ethnically and socioeconomically diverse sample. *Early Child Dev Care* 2008:1-18.
18. Grogan-Kaylor A, Otis MD. The predictors of parental use of corporal punishment. *Family relations* 2007;56:80-91.
19. Berg-Nielsen TS, Vikan A, Dahl AA. Parenting related to child and parental psychopathology: a descriptive review of the literature. *Clin Child Psychol Psychiatry* 2002;7:529-552.
20. McLearn KT, Minkovitz CS, Strobino DM, Marks E, Hou W. The timing of maternal depressive symptoms and mothers' parenting practices with young children: implications for pediatric practice. *Pediatrics* 2006;118(1):e174-82.
21. Silverstein M, Augustyn M, Young R, Zuckerman B. The relationship between maternal

depression, in-home violence and use of physical punishment: what is the role of child behaviour? *Arch Dis Child* 2009;94(2):138-43.

22. Rodriguez CM, Sutherland D. Predictors of parents' physical disciplinary practices. *Child Abuse Negl* 1999;23(7):651-7.
23. Guterman NB, Lee Y, Lee SJ, Waldfogel J, Rathouz PJ. Fathers and maternal risk for physical child abuse. *Child Maltreat* 2009;14(3):277-90.
24. Lee SJ, Bellamy JL, Guterman NB. Fathers, physical child abuse, and neglect: advancing the knowledge base. *Child Maltreat* 2009;14(3):227-31.
25. Lee SJ, Guterman NB, Lee Y. Risk factors for paternal physical child abuse. *Child Abuse Negl* 2008;32(9):846-58.
26. Gardner FE, Sonuga-Barke EJ, Sayal K. Parents anticipating misbehaviour: an observational study of strategies parents use to prevent conflict with behaviour problem children. *J Child Psychol Psychiatry* 1999;40(8):1185-96.
27. Jaddoe VW, van Duijn CM, van der Heijden AJ, Mackenbach JP, Moll HA, Steegers EA, et al. The Generation R Study: design and cohort update until the age of 4 years. *Eur J Epidemiol* 2008.
28. Jaddoe VW, Bakker R, van Duijn CM, van der Heijden AJ, Lindemans J, Mackenbach JP, et al. The Generation R Study Biobank: a resource for epidemiological studies in children and their parents. *Eur J Epidemiol* 2007;22(12):917-23.
29. Straus MA, Hamby SL, Finkelhor D, Moore DW, Runyan D. Identification of child maltreatment with the Parent-Child Conflict Tactics Scales: development and psychometric data for a national sample of American parents. *Child Abuse Negl* 1998;22(4):249-70.
30. *Standaard Onderwijsindeling 2003, Voorburg/Heerlen.* Statistics Netherlands, 2004a.
31. *Allochtonen in Nederland 2004. Voorburg/Heerlen.* Statistics Netherlands, 2004b.
32. Van der Laan AM, Blom M. *Jeugddelinquentie: risico's en bescherming. Bevindingen uit de WODC Monitor Zelfgerapporteerde Jeugdcriminaliteit 2005. [Delinquency in youth: risk and protective factors]* Meppel/Den haag: Boom Juridische uitgevers / Wetenschappelijk Onderzoek- en Documentatiecentrum, 2006.
33. Derogatis LR. *Brief Symptom Inventory (BSI): Administration, scoring and procedures. Manual, third edition.* Minneapolis, MN, USA, 1993.
34. Miller IW, Epstein NB, Bishop DS, Keitner GI. The McMaster Family Assessment Device: Reliability and validity. *J Marital Fam Ther.* 1985;11:345-356.
35. Bernstein DP, Fink L, Handelsman L, Foote J, Lovejoy M, Wenzel K, et al. Initial reliability and validity of a new retrospective measure of child abuse and neglect. *Am J Psychiatry* 1994;151(8):1132-6.
36. WHO. *World Health Organization and International Society for Prevention of Child Abuse and Neglect.*
37. *Preventing Child Maltreatment: A Guide to Taking Action and Generating Evidence.* Geneva, Switzerland, 2006.
38. Belsky J. Psychological maltreatment: Definitional limitations and unstated assumptions. *Dev Psychopathology* 1990;3:31-36.
39. Deater-Deckard K, Dodge KA, Bates JE, Pettit GS. Physical discipline among African American and European American mothers: Link to children's externalizing behaviors. *Dev. Psychol.* 1996;32:1065-1072.
40. Lansford JE, Deater-Deckard K, Dodge KA, Bates JE, Pettit GS. Ethnic differences in the link between physical discipline and later adolescent externalizing behaviors. *J Child Psychol Psychiatry* 2004;45(4):801-12.
41. Berge It, Geurts E. *Opvoeden zonder geweld. Informatie voor ouders en andere opvoeders.* Amsterdam: Nederlands Jeugdinstituut, 2008.

42. Almeida DM, Wethington E, Chandler AL. The transmission of tensions between marital dyads and parent-child dyads. *J Marriage Family* 1999;61:49-61.
43. Krishnakumar A, Beuhler C. Interparental conflict and parenting behaviors: a meta-analytic review. *Family relations* 2000;49:25-44.
44. Galobardes B, Shaw M, Lawlor DA, Lynch JW, Davey Smith G. Indicators of socioeconomic position (part 1). *J Epidemiol Community Health* 2006;60(1):7-12.
45. Galobardes B, Shaw M, Lawlor DA, Lynch JW, Davey Smith G. Indicators of socioeconomic position (part 2). *J Epidemiol Community Health* 2006;60(2):95-101.
46. Beckers I. Negen van de tien vrouwen blijven werken na geboorte kind (Nine out of ten women continues work after childbirth). *Webmagazine Statistics Netherlands.* 2004;December, 2004, Voorburg/Heerlen.
47. Steenhof L. Werkende moeders (working mothers). *Index, Statistics Netherlands.* 2000;No.5, May.
48. Stevens GW, Vollebergh WA. Mental health in migrant children. *J Child Psychol Psychiatry* 2008;49(3):276-294.
49. Bradley RH, Corwyn RF. Socioeconomic status and child development. *Annu Rev Psychol.* 2002;53:371-99.
50. Guterman NB, Lee Y. The role of fathers in risk for physical child abuse and neglect: possible pathways and unanswered questions. *Child Maltreat* 2005;10(2):136-49.
51. Bennett SE, Assefi NP. School-based teenage pregnancy prevention programs: a systematic review of randomized controlled trials. *J Adolesc Health* 2005;36(1):72-81.
52. Vieten C, Astin J. Effects of a mindfulness-based intervention during pregnancy on prenatal stress and mood: results of a pilot study. *Arch Womens Ment Health* 2008;11(1):67-74.
53. Ateah CA, Secco ML, Woodgate RL. The risks and alternatives to physical punishment use with children. *J Pediatr Health Care* 2003;17(3):126-32.

CHAPTER 4

GENERAL DISCUSSION

The general aim of this thesis was to extend the existing knowledge on the relation of social disadvantage with pregnancy outcomes and behaviour early in life. More specifically, we aimed to identify the mechanisms underlying this association. The present chapter highlights our main findings as presented in the previous chapters and provides a discussion of these results in a broader context. Next, I consider some methodological issues. Finally, implications for health policies are discussed.

MAIN FINDINGS

In the first part of this thesis, we studied the association between social disadvantage and different pregnancy outcomes. *Chapter 2.1* described that low maternal educational level, as an indicator of low socioeconomic status (SES), was associated with slower fetal growth resulting in differences in fetal weight. The adverse effect of low education was largest for growth of the fetal head, followed by growth of the fetal femur and abdomen. Maternal smoking during pregnancy and maternal height mediated a large part of educational inequalities in fetal growth characteristics, although inequalities in fetal head circumference remained partly unexplained.

In *chapter 2.2*, we reported that pregnant women with a low educational level had a nearly two-fold higher risk of preterm birth as compared to women with a high educational level. This elevated risk was explained by a combination of several risk factors for preterm birth among women with a low education, such as pre-eclampsia, intrauterine growth retardation, young maternal age, short stature, financial concerns and psychopathology.

In *chapter 2.3*, it was indicated that offspring's birth weight was on average 176 grams lower among the lowest educated women as compared to the highest educated women. A substantial part of the lower birth weight in the offspring of women of low educational level was due to these women's shortened gestational period. The remaining birth weight difference of 126 grams between low and high education was partially attributable to an accumulation of risk factors for low birth weight among low educated women, such as parental height and birth weight, hypertension, maternal age, parity, marital status, unplanned pregnancy, financial difficulties, and most importantly maternal smoking during pregnancy. Despite the contribution of these variables, part of the relationship between educational level and birth weight remained unexplained.

Another indicator of social disadvantage included in this thesis was unemployment. In *chapter 2.4*, we showed that unemployment among pregnant women, as compared to being employed, was associated with a higher risk of several adverse pregnancy outcomes, like small-for-gestational-age and preterm birth. These risks were entirely due to the lower educational level, lower family income and poorer mental health of unemployed women. In contrast, unemployed women had a lower risk of other pregnancy outcomes, mainly involving complications at delivery, than employed women. The lower risk of delivery complications among unemployed

women in our study was attributable to the fact that they were more often multiparous than employed women.

The second part of this thesis provides information on the association between social disadvantage and child behaviour early in life. Sociodemographic and psychosocial determinants of maternal and paternal harsh discipline were also examined in the second part of this thesis. In *chapter 3.1* we showed that several indicators of low SES, such as low parental educational level, low family income and low maternal occupational level, were associated with a more difficult temperament in six months old infants than indicators of high SES. Only the direction of the association between SES and the temperamental scale Depression was reversed. The SES inequalities in the temperamental scales Distress to Limitations, Recovery from Distress, and Duration of Orienting were largely due to young maternal age, single motherhood, family stress and poor maternal psychological well being. These variables could not explain the higher levels of Activity and Fear nor the lower levels of Sadness among infants from low SES groups.

Chapter 3.2 described higher levels of parent-reported behavioural problems in toddlers from various non-Dutch backgrounds as compared to native Dutch children. This relation was partially mediated by maternal psychopathology and indicators of SES. Besides this, we showed that the reported behavioural problems of non-Dutch children were more pronounced among those with unfavourable maternal immigration characteristics, such as poor Dutch language skills and lack of feelings of acceptance by Dutch natives.

Finally, the aim of *chapter 3.3* was to identify determinants of harsh discipline used by mothers and fathers of 3-year old toddlers, since harsh discipline is a well-established risk factor for healthy child development. We showed that psychosocial characteristics of parents, such as psychopathology and stress, were risk factors for use of harsh discipline by both mothers and fathers. Moreover, being a first generation non-Western immigrant consistently predicted harsh discipline in both parents. Indicators of SES, however, were clearly associated with maternal harsh discipline, but hardly with paternal harsh discipline. A substantial part of the association between educational level and maternal harsh discipline was due to other sociodemographic characteristics such as ethnicity, family income, and young maternal age.

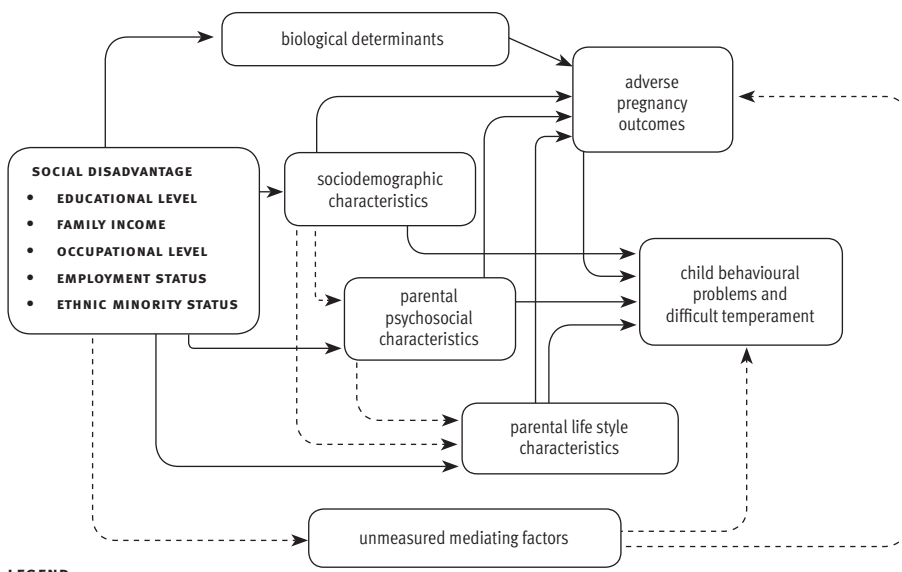
EXPLAINING SOCIAL INEQUALITIES IN PREGNANCY OUTCOMES AND BEHAVIOUR EARLY IN LIFE

In this thesis, large socioeconomic inequalities in pregnancy outcomes were found: women with a low socioeconomic background had an elevated risk of several pregnancy complications as compared to women with a high SES. This confirmed previous studies reporting socioeconomic inequalities in pregnancy outcomes, like preterm birth and low birth weight.[1-13] Equally, in both children and adults, ethnic minority status and low socioeconomic position have repeatedly been associated with mental health problems.[14-19] This social disadvantage gradient has not been observed in very young children so far. We showed that mothers of non-Dutch

origin report more behavioural problems in their toddlers of only 1½-year old as compared to Dutch parents. Moreover, we also documented SES inequalities in temperamental traits in infants of six months of age, a finding that was reported only once before.[20] It is likely that these inequalities are the precursors of the social gradient in behavioural and mental health problems later in life.

In addition to document inequalities in health, the second aim of this thesis was to explain these inequalities. Any effect of social disadvantage on health and behaviour is probably an indirect one, acting through other determinants of the outcome under study, so called mediators. As illustrated in FIGURE 1, different groups of potential mediators were studied: biological determinants, sociodemographic features of the family, and psychosocial and life style related characteristics of the parents. By studying these groups of potential mediators, we aimed to explain the association of social disadvantage with pregnancy complications and behaviour early in life. A variable was only considered as a potential mediator if this variable was known to be associated with both the indicator of social disadvantage and the outcome under study. Therefore, the studied mediators differed per outcome. The biological determinants, for instance, were only studied as possible mediators in the relation between social disadvantage and pregnancy outcomes, and were not examined in relation to child behaviour and parental harsh discipline. Below I discuss the mediating mechanisms per group of mediators.

FIGURE 1. SCHEMATIC REPRESENTATION OF THE POTENTIAL MEDIATING FACTORS IN THE ASSOCIATION OF SOCIAL DISADVANTAGE WITH PREGNANCY OUTCOMES AND CHILD BEHAVIOUR.



BIOLOGICAL DETERMINANTS

We examined whether several biological determinants contributed to the observed educational differences in fetal growth, gestational duration, and birth weight. A previous study examining socioeconomic inequalities in birth weight and preterm birth indicated that *maternal height* mediates part of the association.[21] Our results confirmed this finding. Unlike earlier studies, we examined the role of *parental birth weight* and paternal height in the relation between educational level of pregnant women and birth weight in the offspring. These parental anthropometrics explained a significant part, with maternal and paternal anthropometrics contributing equally to the educational differences in birth weight. Most likely, birth weight and height of both parents can be considered as proxies of a genetic predisposition for fetal growth, birth weight and later length in the offspring.[22]

Hypertension during pregnancy mediated a small but significant part of the educational differences in birth weight. The pathophysiological mechanism underlying the relation of gestational hypertension with fetal growth restriction and decreased birth weight might be reduced placental blood flow or placental vascular damage.[23]

Pre-eclampsia and *intrauterine* growth restriction were mediating factors in the association between educational level and risk of preterm birth. It is well documented that both pre-eclampsia and intrauterine growth restriction are risk factors for preterm birth. A preterm birth can occur spontaneously due to either of these risk factors, but may also be induced to reduce health risks in both mother and child.[24 25]

SOCIODEMOGRAPHIC CHARACTERISTICS

Maternal age was an important factor in the associations between social disadvantage and several outcomes under study. Lower educated women were on average younger during pregnancy. This younger age explained a substantial part of educational inequalities in fetal growth, preterm birth, and birth weight. A young maternal age or more specifically, teenage pregnancy, has repeatedly been associated with an excess risk of poor pregnancy outcomes, including low birth weight and prematurity.[26-28] This association does not only reflect unfavourable sociodemographic and behavioural characteristics of young pregnant women,[28] but also seems to be caused by biological immaturity of teenagers.[26 27] Young maternal age was also an important mediator in the association between educational level and infant temperament, and between national origin and child behavioural problems, which is in accordance with previous studies.[16 29 30]

Women of low SES or non-Dutch background were more often *single parent* than mothers of high SES or Dutch origin. This contributed to the social inequalities in pregnancy outcomes, child behaviour, and use of harsh discipline. There are some explanations for this observation. Single women, in comparison with married or cohabiting women, might have unfavourable living conditions, experience less social support causing elevated levels of stress, and their use of prenatal care may be less optimal. Moreover, it is also likely that single mothers became pregnant unintentionally. Our results indicated that unplanned pregnancies explained part of the educational inequalities in fetal growth and birth weight. Unplanned preg-

nancies might adversely influence fetal growth and birth weight as a result of late onset of prenatal care or due to stress caused by the unexpected pregnancy. Besides, women who did not plan their pregnancy might have had unhealthier life style habits before the pregnancy was known, such as smoking and binge drinking, than women who became pregnant intentionally.

The subjective experience of financial difficulties mediated a substantial part of the educational inequalities in fetal growth, preterm birth, and birth weight. Financial difficulties were strongly correlated with income and might thus be a proxy for low SES. On the other hand, in low as well as in high-income categories numerous participants reported financial strain. *Financial difficulties* might cause adverse pregnancy outcomes through material hardship and lack of money for essential resources, such as healthy food. It is also conceivable that the experience of financial difficulties causes stress.

In chapter 2.2, *maternal educational level* and *family income* were also considered as potential mediators. Ethnic minority status was highly associated with these indicators of SES, while it is known that SES is linked with child behaviour.[14-19] Not surprisingly, maternal educational level and family income contributed to the relation between national origin and child behavioural problems. However, indicators of low SES could not explain the total association between ethnicity and child behavioural problems.

PARENTAL PSYCHOSOCIAL CHARACTERISTICS

In several studies in this thesis, the results confirmed our hypothesis that parental psychosocial characteristics contribute to socioeconomic and ethnic inequalities in pregnancy outcomes and behaviour. The studied psychosocial characteristics were the presence of long lasting difficulties, family stress, and psychosocial well being, as indicated by self-esteem and the presence of psychopathology. Several sociodemographic characteristics, such as single motherhood, unplanned pregnancy, and financial concerns, might also be indications of psychosocial well being, because, hypothetically, these conditions are intertwined with or are indications of psychosocial functioning and stress.

We showed that low educated and unemployed women experienced more *stress* and more *psychopathology*. This partly explained socioeconomic inequalities in adverse pregnancy outcomes, such as slower fetal growth, elevated levels of preterm birth, and lower birth weight in the offspring. Previous research indicated that stress during pregnancy is associated with a relatively high risk of preterm birth and of having a low birth weight infant.[31 32] In these studies it is hypothesized that stress causes these adverse pregnancy outcomes through pregnant women's physiological and hormonal responses to stress.[31 32]

Parental psychosocial characteristics, mostly measured during pregnancy, also contributed significantly to socioeconomic and ethnic inequalities in child behaviour. This may be due to several mechanisms. Firstly, maternal psychological well being during pregnancy may affect growth and brain development of the fetus. For example, Teixeira and colleagues[33] reported that maternal anxiety during

pregnancy was associated with reduced blood flow through the uterine arteries, which affects fetal development. Chronic maternal stress in pregnancy may also expose the fetus to increased levels of stress hormones.[34] Adaptation of the fetus to this 'stressful' fetal environment possibly influences the development of stress systems.[34] Secondly, since psychosocial circumstances during and after pregnancy are highly associated [35], maternal psychosocial well being as measured during pregnancy might also affect child behaviour due to impaired interaction between the mother and her child early in life. Finally, reporter bias is a possible explanation, because a parent report of child behaviour may reflect the well being of both the child and the reporting parent.

Chapter 3.2 showed that, within the mother-child dyads of non-Dutch origin, mothers with several *immigration risk factors* reported more behavioural problems in their toddlers than mothers with only a few immigration risk factors. As the immigration characteristics largely reflected the degree to which a mother had become acquainted with and felt comfortable in the Dutch society, I hypothesize that maternal immigration characteristics affect child behaviour mostly through stress as experienced by the mothers.

MATERNAL LIFE STYLE CHARACTERISTICS

Several studies in this thesis examined whether parental life style characteristics during pregnancy contributed to educational inequalities in pregnancy outcomes. Of the potential mediators studied in this thesis, *smoking habits* of pregnant women explained by far the largest part of the socioeconomic differences in fetal growth and birth weight. Previously, Finnish research[8] also indicated that smoking explained up to half the excess risk for low birth weight in the lowest socioeconomic group. The effect of smoking on fetal growth might be direct with products of cigarette smoke, such as carbon monoxide, tar and nicotine, affecting fetal development.[36] Indirect effects of smoking include maternal and fetal undernutrition, or fetal hypoxia due to vasoconstriction in the placenta.[37 38] In contrast to our findings regarding fetal growth and birth weight, smoking during pregnancy contributed only minimally to the excess risk of preterm birth among low educated and unemployed women as compared to women with a high education or paid employment. We also studied the influence of maternal smoking during pregnancy on child behaviour. Smoking prevalence during pregnancy did not contribute to socioeconomic differences in infant temperament. However, part of the ethnic inequalities in child behavioural problems was due to differences in smoking prevalence during pregnancy between Dutch and non-Dutch mothers. The above described effects of smoking on fetal (brain) development might be the cause of later child behavioural problems.[36-38] An alternative explanation for the association of smoking during pregnancy with behaviour in the offspring might be epiphenomena of smoking, as smoking co-occurs with psychopathology and abuse of other substances.[39 40]

Within the Generation R Study, continuation of *alcohol consumption* during pregnancy was relatively more common among women with a high socioeconomic

background as compared to women of low SES. The amount of alcoholic drinks consumed was, however, on average fairly low. In the first trimester of pregnancy, 2.4% of the women participating in our study drank one or more alcoholic consumptions per day. This percentage decreased to 0.5% in the third trimester of pregnancy. Adjusting for alcohol consumption led to a reduction in the risk of preterm birth among lower educated women. It is hypothesized that low to moderate alcohol consumption during pregnancy may be genuinely beneficial in preventing preterm birth. However, the effects may also be explained by the 'healthy drinker effect', in which women with a poor obstetric history are more likely to abstain from drinking.[41] Alcohol consumption did not contribute to socioeconomic differences in birth weight.

Body mass index (BMI) of the pregnant women was studied as well. With regard to birth weight, BMI had an opposite effect than the other mediators under study: BMI did not explain educational inequalities in birth weight, but had a protective effect. The explanation for this finding is that lower educated women had on average a higher BMI than high educated women, while BMI is positively correlated with birth weight.[22] It can be argued that, if low educated women had the same mean BMI as high educated women, then the average birth weight in the offspring of low educated women would even be lower. In contrast to the protective effect on birth weight, BMI clearly explained part of the increased risk of preterm birth among lower educated women and unemployed women. Overweight is associated with an increased risk of diabetes gravidarum in pregnant women and with macrosomia in the offspring.[42] These conditions possibly lead to preterm birth, either spontaneous or induced.[43]

ALTERNATIVE EXPLANATIONS FOR THE ASSOCIATION OF SOCIAL DISADVANTAGE WITH PREGNANCY OUTCOMES AND EARLY CHILDHOOD BEHAVIOUR

The mediators studied in this thesis did not account for all observed social inequalities in pregnancy outcomes and child behaviour. Several factors could be examined as potential pathways in future research.

Information on nutrition during pregnancy was not available at the time the studies in this thesis were conducted. Research among pregnant women indicated that SES was positively associated with fruit, vegetable and fish consumption and inversely related to intake of high-fat foods.[44-46] Nutrition has been linked with pregnancy outcomes. Valero De Bernabe and colleagues[47] pointed out that pregnant women need additional energy intake (approximately 300 kcal per day) to achieve optimal fetal growth. The intake of specific nutrition components, like proteins, vitamins, and omega-3 fatty acids, has also beneficial effects on birth weight.[31 47] Dietary patterns of pregnant women might thus contribute to the observed socioeconomic inequalities in fetal growth (*chapter 1.1*) and birth weight (*chapters 1.3 and 1.4*).

Possibly, genetic factors underlie differences in fetal growth, birth weight, temperament, and behaviour between socially advantaged and disadvantaged children. Although we accounted for several proxies of heritability, such as parental birth weight, height and psychopathology, it is unlikely that these concepts cover all genetic predispositions for offspring's birth weight and behaviour. If genes related to growth and mental health vary by SES or ethnicity,[48 49] then genetic factors might contribute to the social disadvantage gradient in birth weight and behavioural problems. This merits further investigation and is possible in the Generation R Study once the genetic profiles of the participants become available.

Early environmental influences might account for part of the relation of social disadvantage with temperament and behaviour early in life. It is likely that feeding practices, sleeping patterns, parental soothing behaviour, maternal work (hours), and day care attendance differ between various socioeconomic and ethnic groups. These factors may influence temperament and behaviour early in life, and thereby contribute to temperamental and behavioural inequalities between children of socially advantaged and disadvantaged backgrounds.

There are also other potential reasons for the ethnic differences in child behavioural problems, which might also contribute to ethnic differences in parental harsh discipline. Dissimilar expectancies and beliefs across cultures concerning appropriate child behaviour could influence a parents' report of child behaviour.[50] Equally, ideas about the effectiveness of harsh discipline may also differ between cultural groups leading to ethnic differences in harsh discipline. Another possible explanation for the remaining ethnic inequalities in children's behavioural problems and in parental harsh discipline is that non-Dutch families experience more stress than native Dutch families. Parental stress influences the behaviour of the offspring.[51] Likewise, stress might also lead to elevated levels of harsh discipline. Although some stress related factors were included in our analyses, we did not account for other indicators of stress that are specifically associated with ethnic minority status. Future research should target stress related factors such as discrimination, integration problems, the experience of traumatic events before and during immigration, and living in disadvantaged neighbourhoods.

Finally, it is established that the use of harsh discipline influences child behaviour.[52 53] We showed that parents of non-Dutch or low socioeconomic background, as compared to Dutch parents or parents with a high SES, were more likely to use harsh discipline. Hypothetically, harsh discipline mediates the association between social disadvantage and child behavioural problems. This hypothesis can be examined if the data collection within Generation R on child behaviour at the age of five years is completed.

METHODOLOGICAL CONSIDERATIONS

The strengths and limitations of the separate studies have been described in the specific chapters. Here, I will discuss some general methodological considerations that pertain to studies aimed at unraveling the mechanisms underlying social inequalities in health.

Selection bias

All pregnant women living in the study area in Rotterdam with an expected delivery date between April 2002 and January 2006 were invited to participate in the Generation R Study. The initial response rate was estimated at 61%. Non-participation was not random: pregnant women from ethnic minority groups and lower socioeconomic backgrounds were underrepresented in our study.[54] Typically, most population based cohort studies are confronted with this problem.[55-57] Nevertheless, it raises the question whether selection bias has limited the generalizability of our findings. Selection bias occurs if an association between determinant and outcome differs between those who participate and those who were eligible for the study, but did not participate. In a recent study, participants of the Danish National Birth Cohort Study were compared with non-participating persons.[58] Effect estimates for associations between well-established risk factors and pregnancy outcomes were quite comparable between the two groups, indicating that bias due to non-participation was rather small. Given the similarities in the designs of the Danish National Birth Cohort Study and the Generation R Study, these results suggest that selective participation did not influence our findings to a large extent either, which implies that the results presented in this thesis may be generalized to the general population.

The studies described in this thesis also suffered from selective non-response to postal questionnaires, leading to missing data on determinants, outcomes and covariates. We repeatedly indicated that data was more complete in higher educated, non-single, Dutch mothers, who experienced less psychopathological symptoms. This selective response resulted in an under-representation of pregnant women and children of the most disadvantaged groups, who are at increased risk for adverse pregnancy outcomes and behavioural problems. To overcome part of this problem, we applied imputation techniques in several studies to impute missing information on the covariates. Participants with missing data on determinant or outcome were, however, excluded in the separate studies. This may have affected our results if the relation between determinants and outcomes differed between responding and non-responding families. Since this is, however, mostly unknown, I can only contemplate about the effect of selective response.

Information bias

Information bias occurs if misclassification of the outcome is related to the determinant, or vice versa. Self-reported data are particularly prone to misclassification.[59] Information on the outcomes described in chapter 3 and on all determinants was obtained by parental questionnaires. Differential misclassification of

educational level, household income, occupation and ethnic origin is unlikely, as information on these determinants was collected before assessment of the outcomes. Nevertheless, misclassification due to the use of parent-reported data on children's temperament and behaviour is likely. Zwirs and colleagues[60] showed, for instance, that parents of Turkish, Moroccan and Surinamese background tended to underreport behavioural problems in their children. This indicates that the associations between national origin and behavioural problems may well be larger than observed in our study (*chapter 3.2*). Future studies should use independent observers or obtain information from day nurseries and playgroups to complement our findings on social inequalities in parent-reported child behaviour. Misclassification might also have occurred in our study on harsh discipline (*chapter 3.3*). If Dutch parents are more aware of the taboo on use of harsh discipline in the Netherlands than non-Dutch parents,[61] social desirability may have influenced the reports of Dutch parents to a larger extent than reports of parents of other national origins. This would have led to an overestimation of the association between ethnicity and harsh discipline.

Information on several potential mediators, such as lifestyle habits (smoking and alcohol consumption), psychopathological symptoms and stress, was also obtained by parental questionnaires. This may have introduced misclassification as well. Literature on the accuracy of self reported health behaviours suggests that respondents tend to underreport characteristics that are considered to be undesirable or negative; this is more pronounced among persons with a low educational level.[62 63] Due to this phenomenon, the contribution of some mediators to the explanation of social inequalities in health is perhaps underestimated.

Measurement of socioeconomic status

In several studies presented in this thesis, we focussed on socioeconomic status as an indicator of social disadvantage. Socioeconomic status (SES) is a multidimensional construct pertaining to economic resources and to the position an individual holds within the structure of society regarding prestige and knowledge.[64 65] This implies that there are several ways to assess SES.

Educational level, occupational level, and household income are all commonly used to estimate an individual's SES. Other less frequently used indicators of SES are material hardship, being medically uninsured, and car ownership. Indicators of SES can be studied separately, but can also be combined into a composite measure that reflects multiple socioeconomic factors. However, few of these composite measures have been validated.[64] Moreover, and perhaps even more importantly, education, occupation and household income represent different aspects of SES and therefore might have different associations with different health outcomes.[64-66] Additionally, studying indicators of SES separately makes findings easier to comprehend. For these reasons, we studied indicators of SES separately.

Since levels of education, occupation or income are not applicable to children, parental socioeconomic indicators are applied to estimate the level of SES of a child.[67 68] In our study, maternal and paternal educational level were defined

by the highest educational attainment and categorized according to a standard classification system of Statistics Netherlands.[69] Otherwise, it is also possible to express educational level in the number of years of schooling, which seems to make interpretations and generalizations across countries easier.[65] The number of years of schooling, however, does not necessarily contain information about the required cognitive abilities, knowledge and skills or the quality of the education.[67 68] Occupational level was defined by the level of education that was required for a specific profession (*chapter 3.1*). Although this obviously resulted in a high correlation between the two concepts, only 32% of the participants had a matching educational and occupational level. We also used employment status, i.e. employed versus unemployed, as an indicator of SES (*chapter 1.4*). Family income was defined by the total net monthly income of the household.[70] The multiple-choice answering categories -12 categories ranging from below 450 euro's to more than 2200 euro's consisted of small units in order to gain accurate information on income. The chosen categories showed, however, a ceiling effect with 55% of the participants in the highest income category, since our study population consisted primarily of two-income families. Therefore, we combined categories into <1200, 1200-2000, and >2000 euro's monthly household income.

Educational level of the mother was used as the primary indicator of the child's SES. Previously, in both Western and developing countries, maternal education has been indicated as the strongest socioeconomic marker of pregnancy outcomes and child health.[71] Our results are in line with this: of all studied SES indicators, maternal education showed the strongest association with fetal growth, infant temperament and maternal harsh discipline. Possibly, education reflects material resources as it structures occupation and income, while it also reflects non-economic social characteristics, such as general and health-related knowledge, literacy, problem-solving skills and prestige.[67 68] These characteristics probably result in a wide range of favourable behaviours that play a role in child health. For instance, access to care is in principal equal in the Netherlands, but well-educated women may be more likely to engage in health-seeking behaviour, start earlier with prenatal care or may optimise their use of health services through better communication with health care professionals.[67 68 72] It is also suggested that income and occupational level are better indicators of SES than educational level, because educational attainment is rather static.[70] SES changes over time and is perhaps better reflected by dynamic entities such as income or occupation. This may, however, apply mainly to persons who are in the workforce for numerous years, while our study population of parents(-to-be) was on average rather young and typically started working only a few years ago.

STATISTICAL MODEL

In this thesis, regression adjustment was used to assess mediation mechanisms in the association between social disadvantage and health.[73 74] Briefly, this method, also known as the decomposition approach, comprises of two consecutive regression analyses. Firstly, unadjusted (or confounder adjusted) effect estimates are cal-

culated. Next, the regression analysis is repeated including one or more risk factors that are hypothesized to mediate the effect of social disadvantage on health and behaviour. The difference between the effect estimates of the first and second analysis reflects how much of the effect of social disadvantage on the outcome under study is mediated by a certain risk factor.

The use of regression adjustment to assess mediation mechanisms has some limitations. Firstly, regression adjustment is based on the assumption that a mediator is on the causal pathway between an exposure –social disadvantage in our case– and the outcome. As this required assumption on causality is often difficult to verify, potential mediators were carefully selected based on existing knowledge and theoretical frameworks. Secondly, regression adjustment has been criticized, because the percentage of change can be similar for different absolute changes in effect estimates. Expressing estimates in standard deviation scores can partially solve this issue. This, however, would make interpretation of the regression coefficients less comprehensible.

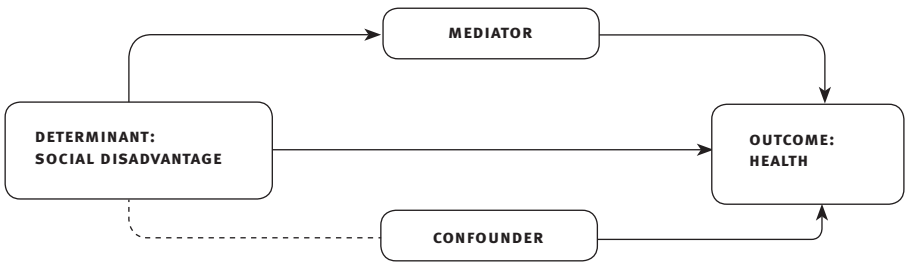
Due to these limitations, researchers have suggested to use alternative methods, such as structural equation modelling or path analysis.[75 76] These methods, nevertheless, have the same problems regarding causality and are also limited by the assumption of absence of effect modification.[77] Hence, as alternative methods are not necessarily better, regression adjustment remains the most widely used approach to assess the contribution of risk factors to social inequalities in health.

CONFOUNDING AND MEDIATING

In epidemiological research, it is common to consider the role of third variables (covariates), once a relationship between two variables has been identified.[78 79] As our aim was to examine mechanisms underlying social inequalities in health, the focus of this thesis was on a specific kind of covariates, so called '*mediators*'. If an association between a determinant and outcome has been established, the following conditions must be fulfilled for variables to be a mediator (FIGURE 2):[78 79]

1. Determinant must be causally related to the mediator.
2. The mediator must be must be causally related to the outcome under study.
3. The relation between the determinant and the outcome must attenuate after controlling for the mediator.

FIGURE 2. MEDIATORS AND CONFOUNDERS IN THE ASSOCIATION BETWEEN DETERMINANT AND OUTCOME.



Based on pre-existing knowledge, we selected potential mediators that fulfilled conditions 1 and 2. Next, the third condition was tested. In *chapter 2.3*, covariates were regarded as mediators if the change in effect estimates of the association between educational level and birth weight was statistically significant (level of significance was set at 0.10).[80 81] In the other chapters, variables were considered mediators if they led to a change of more than 5% in the effect estimates of the relation between social disadvantage and an outcome.[80] The threshold (change <5% or p-value<0.10) was rather non-conservative to ensure that small mediation effects were also included.

In all studies, we also considered another type of covariates, namely confounding factors that may have obscured or accentuated the association between social disadvantage and health. Confounders fulfill the same criteria as mediators, except that condition 1 is different: the determinant should not be causally related to a confounder. So, a causal relation between determinant and confounder should be absent, but it might also be that the confounder causes the determinant. Confounding factors were selected using the same method as for mediators, i.e. conditions 1 and 2 based on previous research and condition 3 by calculating the change in effect estimates of the main association under study.

Since confounders and mediators require the same statistical approach, the difference between both variables is only conceptual. The decision on the nature of covariates was sometimes complicated. This was, for instance, particularly true for the variable maternal age. As the association between social disadvantage and maternal age is not necessarily causal, maternal age was sometimes considered as a confounder (*chapter 1.2*). Nevertheless, social disadvantage might also influence the age at which women get pregnant, i.e. that low SES or ethnic minority women want to have children at a younger age than high SES or native women. Therefore, maternal age was also regarded as a potential mediator in several chapters (*2.3, 3.1 and 3.2*).

REVERSE CAUSALITY

Another issue that may have hampered our studies is reverse causality.[70] This pertains to the first condition of the mediation criteria as presented in the preceding section, i.e. the assumption that social disadvantage is causally related to the mediator. There is the possibility that relations between social disadvantage and presumed mediators were causal in a reverse way. To take the example of maternal age again, it is conceivable that becoming pregnant at a young age partly determines a women's educational attainment, as women below a certain age cannot be expected to have completed university.

Below, I will discuss the issue of reverse causality for the association between SES and some of the mediators studied in this thesis. Firstly, parity might influence the SES-indicators family income and occupational level as follows: parents work on average less than men and women without children,[82 83] which causes a reduced family income and may also influence occupational level, for instance due to delayed promotions. Moreover, it is also known that the up bringing of children

is expensive: the monthly income has to be divided over an extra person, whereby a lack of money may arise. Secondly, parental height can affect SES-indicators in the following way: it has been reported that taller persons are more successful in their careers than persons with a short stature, thereby parental height might influence family income and occupational level.[84] Thirdly, marital status influences household income as well: single women have their own income, which is probably lower than the income of men and women together. Fourthly, psychopathology might act upon SES like this: enduring psychopathological symptoms can bring about unemployment or being unable to work,[85-89] which might eventually cause a lower income. Moreover, as it has been reported that anxiety and depression during teenage years are associated with early school drop out,[87-89] psychopathological symptoms with an early onset might thus have influenced educational attainment as well.

Reverse causality should also be considered in the association of national origin with SES and psychopathology. This specifically concerns first generation immigrants and is less relevant for second or third generation immigrants. Although I assumed that ethnic minority status leads to low SES, it is also known that low educational attainment, low income, low occupational level or unemployment predisposes to immigration.[90] Equally, psychopathology might also predispose to immigration, thereby causing elevated levels of psychopathology in immigrants as compared to native Dutch persons.[91 92]

Obviously, these examples of reverse causality may be relevant for some, but certainly not for all participants in our study. Though, the mediated proportion of the associations between social disadvantage and health that were ascribed to certain mediators might be slightly overestimated.

IMPLICATIONS FOR PREVENTION AND INTERVENTION

Health inequalities between socially advantaged and disadvantaged people are widespread and seem to involve the whole spectrum of health and disease. It is obvious that the prevention of these undesirable health inequalities is a global public health goal. As indicators of social disadvantage, such as low socio-economic status and ethnic minority status, are not easily amendable, prevention and intervention programs should be aimed at the mechanisms underlying the association between social disadvantage and health and disease.

We showed that pregnancy complications and child behavioural problems in socially disadvantaged families were partially due to an accumulation of adverse circumstances in these families. Except for maternal smoking during pregnancy, which explained almost half of the inequalities in birth weight, the mediating factors separately explained on average between 5% and 20% of social inequalities in the outcome under study. Therefore, interventions are likely to have the greatest impact if focused on a combined approach to reduce the prevalence of several risk factors in the most disadvantaged groups. Even though some risk factors for

adverse outcomes among low educated women, such as short stature, may not be easily amendable, other risk factors provide a window of opportunity for intervention strategies to reduce social inequalities in pregnancy complications and child behavioural problems.

Before discussing the preventive measures and interventions for the separate amendable risk factors, I would like to stress that interventions must be accessible for pregnant women with social disadvantage. This is a major challenge as ethnic minority groups and individuals of low socioeconomic status are often difficult to reach. These groups enroll later in pregnancy health care and make less use of health care offered during early childhood.[93] Regarding the proposed preventive measures and interventions (see below), efforts should be made to approach socially disadvantaged target groups in various ways prior to conception, during pregnancy and in early childhood. The recently launched campaign to reduce perinatal mortality in Rotterdam ("Aanvalsplan perinatale sterfte") suggested that the social network of individuals, for instance social and religious meeting places, sport clubs and shops, should be used to get socially disadvantaged individuals more acquainted with the Dutch health care facilities.[94] Furthermore, adolescents of various backgrounds can be reached via schools and it should be examined whether supplemental intervention measures in vocational training and other low level educations reduce the number of adolescent pregnancies. Finally, the recently founded youth health care centres (Centra voor Jeugd en Gezin) have the policy to reach out to the community: if parents miss a visit and do not respond to invitations, health care workers will visit the family at home. In this way, families of socially disadvantaged backgrounds might be reached more often.

Almost half of the educational inequalities in birth weight of the offspring was attributable to smoking during pregnancy. This was the result of a relatively high percentage (38%) of lower educated women that continued to smoke during pregnancy as compared the highest educated women (5%). So, altering smoking habits may be an option to reduce educational differences in fetal growth and birth weight. Of the interventions aimed at smoking cessation during pregnancy, brief counseling by the prenatal care giver is most frequently applied, as it is a cost-effective intervention.[95 96] In the Netherlands, prenatal care typically starts at the end of the first trimester.[97] Part of the first visit to the gynaecologist or midwife is aimed at health education, e.g. about the harmful consequences of smoking during pregnancy. In general, this counseling leads to cessation in about 5% to 10% of pregnant women.[95] As individuals of low SES, as compared to persons with a high SES, are less successful in smoking cessation,[98] it might be that socially disadvantaged women need more than the standard counseling that is given now. Prenatal care providers must be aware that especially women with a low SES tend to continue smoking during pregnancy. Additionally, nationwide campaigns could raise awareness about the detrimental effects of smoking on maternal and fetal health. Sociodemographic risk factors, such as young maternal age and single motherhood, explained part of the risk of pregnancy complications, of more difficult

child behaviour and of use of harsh discipline among socially disadvantaged women. Young maternal age and single motherhood are probably associated with poor material circumstances, delayed start or less optimal use of prenatal care, elevated levels of stress, less social support, and unhealthy behaviours like smoking. Socially disadvantaged women also experienced more stress and psychopathology than socially advantaged women, which contributed to the risk of pregnancy complications and difficult child behaviour among socially disadvantaged women. Increased awareness of prenatal caregivers and child health care workers in signaling risk factors associated with social disadvantage, such as maternal psychosocial problems, young maternal age, and single motherhood, might result in higher enrollment rates of socially disadvantaged mothers(-to be) in therapy or social support programs. Research suggests that social support programs are effective in diminishing the risks of adverse pregnancy outcomes and child well being.[99] [100] It is thought that these social support programs improve well being of mother and child through counseling, helping women to enlarge their social network, accomplishing continuation of prenatal care, and by affecting life style behaviours positively.

In *chapter 3.2*, immigration risk factors of mothers of non-Dutch origin were associated with increased levels of child behavioural problems. Apparently, processes associated with immigration and integration are not only of importance to first-generation immigrants, but also affect the well being of next-generation offspring. This merits extra attention, as the number of immigrants in most Western countries is still increasing rapidly. Our results underline the significance for immigrants to learn the host country's language, and to become acquainted with and feel at home in the host country. Although this implies that immigrants should, to some extent, adjust to the host country, it also means that a host country must give immigrants the opportunity to integrate within the society.

An essential issue in these suggested intervention programs is the timing of implementation. Interventions aimed at risk factors for pregnancy complications should be applied as early in pregnancy as possible. Equally, for efforts aimed at the prevention of child behavioural problems or parental harsh discipline to be effective, interventions should be initiated early in children's lives or even already during pregnancy. However, it would probably even be more effective to embed intervention programs in preconception care.[101] In this way, women can already quite smoking or can seek help for their psychosocial problems ahead of becoming pregnant. Awareness about the risks associated with pregnancy at a young age or single motherhood could be increased by nation wide, school based campaigns. To reduce social inequalities in health, preconception care and prevention campaigns should be specifically aimed at reaching socially disadvantaged women.

CONCLUSIONS

The studies in this thesis indicated that a large social gradient exists in pregnancy outcomes in women living in Rotterdam, the Netherlands: women with a low socioeconomic background, as compared to women with a high SES, had an elevated risk of adverse pregnancy outcomes, such as slower fetal growth, preterm birth, and low birth weight. A substantial part of the inequalities was due to an accumulation of risk factors for adverse pregnancy outcomes among socially disadvantaged women. Important mediating factors were height and birth weight of pregnant women and their partners, smoking during pregnancy and indicators of stress and psychosocial problems among pregnant women.

Equally, we found a large social gradient in behaviour early in life with infants of low SES displaying more temperamental difficulties and toddlers of non-Dutch origin having higher levels of parent-reported behavioural problems. This gradient was also observed in parenting style with parents of low SES or non-Dutch origin being more likely to harshly discipline their 3-year old child than parents of high SES or Dutch background. The main mediating factors in these relations were sociodemographic risk factors, such as young parental age and single motherhood, and indicators of stress and psychosocial problems of the parents. We also showed that maternal immigration characteristics, such as Dutch language skills and feelings of acceptance by the Dutch society, are associated with behavioural problems among toddlers of non-Dutch origin.

In conclusion, despite overall increases in prosperity in the Netherlands, there are still marked social inequalities in pregnancy outcomes and behaviour early in life. Although we explained a substantial part of the social inequalities, we were unable to explain all differences in pregnancy outcomes and child behaviour between families of socially advantaged and disadvantaged backgrounds. The observed social inequalities early in life are most likely precursors of the social gradient in health and disease later in life. Hence, it is important that future research aims to further disentangle social inequalities in pregnancy outcomes and child behaviour. In the meanwhile, I recommend the development and implementation of effective public health interventions to reduce undesirable social inequalities in health and behaviour early in life.

REFERENCES

1. Koupilova I, Bobak M, Holcik J, Pikhart H, Leon DA. Increasing social variation in birth outcomes in the Czech Republic after 1989. *Am J Public Health.* 1998;88(9):1343-7.
2. Luo ZC, Kierans WJ, Wilkins R, Liston RM, Mohamed J, Kramer MS. Disparities in birth outcomes by neighborhood income: temporal trends in rural and urban areas, british columbia. *Epidemiol.* 2004;15(6):679-86.
3. Mackenbach JP. Socio-economic health differences in The Netherlands: a review of recent empirical findings. *Soc Sci Med.* 1992;34(3):213-26.
4. Moser K, Li L, Power C. Social inequalities in low birth weight in England and Wales: trends and implications for future population health. *J Epidemiol Community Health.* 2003;57(9):687-91.
5. Clausen T, Oyen N, Henriksen T. Pregnancy complications by overweight and residential area. A prospective study of an urban Norwegian cohort. *Acta Obstet Gynecol Scand* 2006;85(5):526-33.
6. Haelterman E, Qvist R, Barlow P, Alexander S. Social deprivation and poor access to care as risk factors for severe pre-eclampsia. *Eur J Obstet Gynecol Reprod Biol* 2003;111(1):25-32.
7. Ancel PY, Saurel-Cubizolles MJ, Di Renzo GC, Papiernik E, Breart G. Social differences of very preterm birth in Europe: interaction with obstetric history. Europop Group. *Am J Epidemiol* 1999;149(10):908-15.
8. Gissler M, Merilainen J, Vuori E, Hemminki E. Register based monitoring shows decreasing socioeconomic differences in Finnish perinatal health. *J Epidemiol Community Health.* 2003;57(6):433-9.
9. Luo ZC, Wilkins R, Kramer MS. , Fetal and Infant Health Study Group of the Canadian Perinatal Surveillance System. Effect of neighbourhood income and maternal education on birth outcomes: a population-based study. *CMAJ* 2006;174(10):1415-20.
10. Meis PJ, Michielutte R, Peters TJ, Wells HB, Sands RE, Coles EC, et al. Factors associated with preterm birth in Cardiff, Wales. I. Univariable and multivariable analysis. *Am J Obstet Gynecol.* 1995;173(2):590-6.
11. Aszkenasy M, Hutchison S. Births, gestation and birthweights in South Tees 1990-1996. *J Public Health Med* 2000;22(4):457-61.
12. Peacock JL, Bland JM, Anderson HR. Preterm delivery: effects of socioeconomic factors, psychological stress, smoking, alcohol, and caffeine. *BMJ.* 1995;311(7004):531-5.
13. Smith LK, Draper ES, Manktelow BN, Dorling JS, Field DJ. Socioeconomic inequalities in very preterm birth rates. *Arch Dis Child Fetal Neonatal Ed* 2007;92(1):F11-4.
14. Caspi A, Taylor A, Moffitt TE, Plomin R. Neighborhood deprivation affects children's mental health: environmental risks identified in a genetic design. *Psychol Sci.* 2000;11(4):338-42.
15. Kahn RS, Wilson K, Wise PH. Intergenerational health disparities: socioeconomic status, women's health conditions, and child behavior problems. *Public Health Rep.* 2005;120(4):399-408.
16. Kalff AC, Kroes M, Vles JS, Hendriksen JG, Feron FJ, Steyaert J, et al. Neighbourhood level and individual level SES effects on child problem behaviour: a multilevel analysis. *J Epidemiol Community Health.* 2001;55(4):246-50.
17. Reijneveld SA, Brugman E, Verhulst FC, Verloove-Vanhorick SP. Area deprivation and child psychosocial problems–a national cross-sectional study among school-aged children. *Soc Psychiatry Psychiatr Epidemiol.* 2005;40(1):18-23.
18. Maughan B, Collishaw S, Meltzer H, Goodman R. Recent trends in UK child and adolescent mental health. *Soc Psychiatry Psychiatr Epidemiol* 2008;43(4):305-10.
19. Tick NT, van der Ende J, Verhulst FC. Ten-year trends in self-reported emotional and behavioral problems of Dutch adolescents. *Soc Psychiatry Psychiatr Epidemiol* 2008.

20. Sameroff AJ, Seifer R, Elias PK. Sociocultural variability in infant temperament ratings. *Child Dev* 1982;53(1):164-73.
21. Raum E, Arabin B, Schlaud M, Walter U, Schwartz FW. The impact of maternal education on intrauterine growth: a comparison of former West and East Germany. *Int J Epidemiol.* 2001;30(1):81-7.
22. Kramer MS. Intrauterine growth and gestational duration determinants. *Pediatrics.* 1987;80(4):502-11.
23. Maulik D. Fetal growth restriction: the etiology. *Clin Obstet Gynecol* 2006;49(2):228-35.
24. Duley L, Meher S, Abalos E. Management of pre-eclampsia. *Bmj* 2006;332(7539):463-8.
25. Hershkovitz R, Erez O, Sheiner E, Bashiri A, Furman B, Shoham-Vardi I, et al. Comparison study between induced and spontaneous term and preterm births of small-for-gestational-age neonates. *Eur J Obstet Gynecol Reprod Biol* 2001;97(2):141-6.
26. Fraser AM, Brockert JE, Ward RH. Association of young maternal age with adverse reproductive outcomes. *N Engl J Med* 1995;332(17):1113-7.
27. Smith GC, Pell JP. Teenage pregnancy and risk of adverse perinatal outcomes associated with first and second births: population based retrospective cohort study. *Bmj* 2001;323(7311):476.
28. Cunnington AJ. What's so bad about teenage pregnancy? *J Fam Plann Reprod Health Care.* 2001;27(1):36-41.
29. Bradley RH, Corwyn RF. Socioeconomic status and child development. *Annu Rev Psychol.* 2002;53:371-99.
30. Kalff AC, Kroes M, Vles JS, Bosma H, Feron FJ, Hendriksen JG, et al. Factors affecting the relation between parental education as well as occupation and problem behaviour in Dutch 5- to 6-year-old children. *Soc Psychiatry Psychiatr Epidemiol* 2001;36(7):324-31.
31. Hobel C, Culhane J. Role of psychosocial and nutritional stress on poor pregnancy outcome. *J Nutr.* 2003;133(5 Suppl 2):1709S-1717S.
32. Mulder EJ, Robles de Medina PG, Huizink AC, Van den Bergh BR, Buitelaar JK, Visser GH. Prenatal maternal stress: effects on pregnancy and the (unborn) child. *Early Hum Dev.* 2002;70(1-2):3-14.
33. Teixeira JM, Fisk NM, Glover V. Association between maternal anxiety in pregnancy and increased uterine artery resistance index: cohort based study. *Bmj* 1999;318(7177):153-7.
34. Gitau R, Cameron A, Fisk NM, Glover V. Fetal exposure to maternal cortisol. *Lancet* 1998;352(9129):707-8.
35. Milgrom J, Gemmill AW, Bilszta JL, Hayes B, Barnett B, Brooks J, et al. Antenatal risk factors for postnatal depression: a large prospective study. *J Affect Disord* 2008;108(1-2):147-57.
36. Slotkin TA. Fetal nicotine or cocaine exposure: which one is worse? *J Pharmacol Exp Ther* 1998;285(3):931-45.
37. Abel EL. Smoking during pregnancy: a review of effects on growth and development of offspring. *Hum Biol* 1980;52(4):593-625.
38. Perkins KA, Sexton JE, DiMarco A, Fonte C. Acute effects of tobacco smoking on hunger and eating in male and female smokers. *Appetite* 1994;22(2):149-58.
39. Hu MC, Davies M, Kandel DB. Epidemiology and correlates of daily smoking and nicotine dependence among young adults in the United States. *Am J Public Health* 2006;96(2):299-308.
40. Degenhardt L, Hall W, Lynskey M. Alcohol, cannabis and tobacco use among Australians: a comparison of their associations with other drug use and use disorders, affective and anxiety disorders, and psychosis. *Addiction* 2001;96(11):1603-14.
41. Henderson J, Gray R, Brocklehurst P. Systematic review of effects of low-moderate prenatal alcohol exposure on pregnancy outcome. *Bjog* 2007;114(3):243-52.
42. Baeten JM, Bukusi EA, Lambe M. Pregnancy complications and outcomes among overweight and obese nulliparous women. *Am J Public Health* 2001;91(3):436-40.

43. Ancel PY, Saurel-Cubizolles MJ, Di Renzo GC, Papiernik E, Breart G. Very and moderate preterm births: are the risk factors different? *Br J Obstet Gynaecol* 1999;106(11):1162-70.
44. Erkkola M, Karppinen M, Jarvinen A, Knip M, Virtanen SM. Folate, vitamin D, and iron intakes are low among pregnant Finnish women. *Eur J Clin Nutr* 1998;52(10):742-8.
45. Whichelow MJ, Prevost AT. Dietary patterns and their associations with demographic, lifestyle and health variables in a random sample of British adults. *Br J Nutr.* 1996;76(1):17-30.
46. Rogers I, Emmett P, Baker D, Golding J. Financial difficulties, smoking habits, composition of the diet and birthweight in a population of pregnant women in the South West of England. ALSPAC Study Team. Avon Longitudinal Study of Pregnancy and Childhood. *Eur J Clin Nutr* 1998;52(4):251-60.
47. Valero De Bernabe J, Soriano T, Albaladejo R, Juarranz M, Calle ME, Martinez D, et al. Risk factors for low birth weight: a review. *Eur J Obstet Gynecol Reprod Biol.* 2004;116(1):3-15.
48. Mackenbach JP. Genetics and health inequalities: hypotheses and controversies. *J Epidemiol Community Health* 2005;59(4):268-73.
49. Holtzman NA. Genetics and social class. *J Epidemiol Community Health* 2002;56(7):529-35.
50. Hackett L, Hackett R. Parental ideas of normal and deviant child behaviour. A comparison of two ethnic groups. *Br J Psychiatry* 1993;162:353-7.
51. Scharf M. Long-term effects of trauma: psychosocial functioning of the second and third generation of Holocaust survivors. *Dev Psychopathol* 2007;19(2):603-22.
52. Gershoff ET. Corporal punishment by parents and associated child behaviors and experiences: a meta-analytic and theoretical review. *Psychol Bull* 2002;128(4):539-79.
53. Larzelere RE. Child outcomes of nonabusive and customary physical punishment by parents: an updated literature review. *Clin Child Fam Psychol Rev* 2000;3(4):199-221.
54. Van Lith H. *Demografische gegevens 2003.* Rotterdam: Center for Research and Statistics (COS), 2004.
55. Galea S, Tracy M. Participation rates in epidemiologic studies. *Ann Epidemiol* 2007;17(9):643-53.
56. Tjonneland A, Olsen A, Boll K, Stripp C, Christensen J, Engholm G, et al. Study design, exposure variables, and socioeconomic determinants of participation in Diet, Cancer and Health: a population-based prospective cohort study of 57,053 men and women in Denmark. *Scand J Public Health* 2007;35(4):432-41.
57. Brown WJ, Bryson L, Byles JE, Dobson AJ, Lee C, Mishra G, et al. Women's Healtth Australia: Recruitment for a National Longitudinal Cohort Study. *Women Health.* 1998;28(23-40).
58. Nohr EA, Frydenberg M, Henriksen TB, Olsen J. Does low participation in cohort studies induce bias? *Epidemiology* 2006;17(4):413-8.
59. Gordis L. Assuring the quality of questionnaire data in epidemiologic research. *Am J Epidemiol* 1979;109(1):21-4.
60. Zwirs BW, Burger H, Buitelaar JK, Schulpen TW. Ethnic differences in parental detection of externalizing disorders. *Eur Child Adolesc Psychiatry* 2006;15(7):418-26.
61. Berge It, Geurts E. *Opvoeden zonder geweld. Informatie voor ouders en andere opvoeders.* Amsterdam: Nederlands Jeugdinstituut, 2008.
62. Wagenknecht LE, Burke GL, Perkins LL, Haley NJ, Friedman GD. Misclassification of smoking status in the CARDIA study: a comparison of self-report with serum cotinine levels. *Am J Public Health* 1992;82(1):33-6.
63. Parna K, Rahu M, Youngman LD, Rahu K, Nygard-Kibur M, Koupil I. Self-reported and serum cotinine-validated smoking in pregnant women in Estonia. *Matern Child Health J* 2005;9(4):385-92.
64. Braveman PA, Cubbin C, Egerter S, Chideya S, Marchi KS, Metzler M, et al. Socioeconomic status in health research: one size does not fit all. *Jama* 2005;294(22):2879-88.
65. Lynch J, Kaplan G. Socioeconomic position. In: Berkman LF, Kawachi I, editors. *Social epidemiology*. New York, USA: Oxford University Press, Inc., 2000.

66. Spencer NJ. Disentangling the effects of different components of socioeconomic status on health in early childhood. *J Epidemiol Community Health* 2005;59(1):2.

67. Galobardes B, Shaw M, Lawlor DA, Lynch JW, Davey Smith G. Indicators of socioeconomic position (part 1). *J Epidemiol Community Health* 2006;60(1):7-12.

68. Galobardes B, Shaw M, Lawlor DA, Lynch JW, Davey Smith G. Indicators of socioeconomic position (part 2). *J Epidemiol Community Health* 2006;60(2):95-101.

69. Christensen U, Lund R, Damsgaard MT, Holstein BE, Ditlevsen S, Diderichsen F, et al. Cynical hostility, socioeconomic position, health behaviors, and symptom load: a cross-sectional analysis in a danish population-based study. *Psychosom Med* 2004;66(4):572-7.

70. Duncan GJ, Daly MC, McDonough P, Williams DR. Optimal indicators of socioeconomic status for health research. *Am J Public Health* 2002;92(7):1151-7.

71. Desai S, Alva S. Maternal education and child health: is there a strong causal relationship? *Demography* 1998;35(1):71-81.

72. Essex C, Counsell AM, Geddis DC. The demographic characteristics of early and late attenders for antenatal care. *Aust N Z J Obstet Gynaecol* 1992;32(4):306-8.

73. Szklo M, Nieto FJ. *Epidemiology: Beyond the basics.* Gaithersburg, MD: Aspen Publishers, 2000.

74. Susser M. *Causal Thinking in the Health Sciences: Concepts and Strategies in Epidemiology.* New York: Oxford University Press, 1973.

75. Susser M, Sergievsky GH, Stein Z. The path analysis approach for the multivariate analysis of infant mortality data. *Ann Epidemiol* 1999;9(1):73-4.

76. Ditlevsen S, Christensen U, Lynch J, Damsgaard MT, Keiding N. The mediation proportion: a structural equation approach for estimating the proportion of exposure effect on outcome explained by an intermediate variable. *Epidemiology* 2005;16(1):114-20.

77. Kaufman JS, MacLehose RF, Kaufman S, Greenland S. The mediation proportion. *Epidemiology* 2005;16(5):710.

78. MacKinnon DP, Krull JL, Lockwood CM. Equivalence of the mediation, confounding and suppression effect. *Prev Sci* 2000;1(4):173-81.

79. Singh-Manoux A. Commentary: Modelling multiple pathways to explain social inequalities in health and mortality. *Int J Epidemiol* 2005;34(3):638-9.

80. MacKinnon D. Contrasts in multiple mediator models. In: Rose JS, Chassin L, Presson CC, Shermon SJ, editors. *Multivariate Applications in Substance Use Research: New Methods for Nem Questions*. Mahwah, NJ: Lawrence Erlbaum, 2000:141-160.

81. Efron B, Tibshirani RJ. *An Introduction to the Bootstrap*. London, UK: Chapman and Hall, 1993.

82. Hynes K, Clarkberg M. Women's Employment Patterns During Early Parenthood: A Group-Based Trajectory Analysis. *J Marriage Family* 2005;67(Februari):222-239.

83. del Boca D, Locatelli M. The Determinants of Motherhood and Work Status: A Survey. *IZA Discussion Paper* 2006;October 2006.

84. Judge TA, Cable DM. The Effect of Physical Height on Workplace Success and Income: Preliminary Test of a Theoreatical Model. *J Applied Psychol* 2004;89(3):428-441.

85. el-Guebaly N, Currie S, Williams J, Wang J, Beck CA, Maxwell C, et al. Association of mood, anxiety, and substance use disorders with occupational status and disability in a community sample. *Psychiatr Serv* 2007;58(5):659-67.

86. Lerner D, Adler DA, Chang H, Lapitsky L, Hood MY, Perissinotto C, et al. Unemployment, job retention, and productivity loss among employees with depression. *Psychiatr Serv* 2004;55(12):1371-8.

87. Schneier FR, Johnson J, Hornig CD, Liebowitz MR, Weissman MM. Social phobia. Comorbidity and morbidity in an epidemiologic sample. *Arch Gen Psychiatry* 1992;49(4):282-8.

88. Turner S, Beidel DC, Epstein LH. Vulnerability and risk for anxiety disorders. *J Anx Disorders* 1991;5:151-166.

89. Wittchen HU, Essau CA, von Zerssen D, Krieg JC, Zaudig M. Lifetime and six-month prevalence of mental disorders in the Munich Follow-Up Study. *Eur Arch Psychiatry Clin Neurosci* 1992;241(4):247-58.

90. Neal Ritchey P. Explanations of migration. *Ann Rev Sociology* 1976;2:363-404.

91. Cochrane R, Bal SS. Migration and schizophrenia: an examination of five hypotheses. *Soc Psychiatry* 1987;22(4):181-91.

92. Hutchinson G, Haasen C. Migration and schizophrenia: the challenges for European psychiatry and implications for the future. *Soc Psychiatry Psychiatr Epidemiol* 2004;39(5):350-7.

93. Newacheck PW, Hughes DC, Stoddard JJ. Children's access to primary care: differences by race, income, and insurance status. *Pediatrics* 1996;97(1):26-32.

94. Rotterdam-Rijnmond G, MC E. Aanvalsplan perinatale sterfte Rotterdam. 2008.

95. Crawford JT, Tolosa JE, Goldenberg RL. Smoking cessation in pregnancy: why, how, and what next. *Clin Obstet Gynecol* 2008;51(2):419-35.

96. Melvin CL, Dolan-Mullen P, Windsor RA, Whiteside HP, Jr., Goldenberg RL. Recommended cessation counselling for pregnant women who smoke: a review of the evidence. *Tob Control.* 2000;9 Suppl 3:III80-4.

97. Wildschut HI, van Vliet-Lachotzki EH, Boon BM, Lie Fong S, Landkroon AP, Steegers EA. [Preconception care: an essential part of the care for mother and child]. *Ned Tijdschr Geneeskd* 2006;150(24):1326-30.

98. Osler M, Prescott E. Psychosocial, behavioural, and health determinants of successful smoking cessation: a longitudinal study of Danish adults. *Tob Control* 1998;7(3):262-7.

99. Rogers MM, Peoples-Sheps MD, Suchindran C. Impact of a social support program on teenage prenatal care use and pregnancy outcomes. *J Adolescent Health* 1996;19(2):132-140.

100. Logsdon MC, Birkimer JC, Ratterman A, Cahill K, Cahill N. Social Support in Pregnant and Parenting Adolescents: Research, Critique, and Recommendations. *J Child Adolesc Psychiatric Nursing* 2007;15(2):75-83.

101. Weerd S, Steegers E. The past and present practices and continuing controversies of preconception care. *Community Genet.* 2002;5(1):50-60.

CHAPTER 5

SUMMARY

SUMMARY

The social position of individuals in a society is associated with health and disease, with socially disadvantaged persons being worst off. The prevention of these health inequalities is a major public health goal. As inequalities in health between socially advantaged and disadvantaged persons are already present early in life and persevere throughout the whole life span, attempts to tackle this gradient should start by reducing socio-economic and ethnic inequalities in fetal life and infancy. However, the indicators of social disadvantage, such as low socio-economic status and ethnic minority status, are not easily amendable. Therefore, it is important to unravel the pathways through which social disadvantage leads to health and disease, because these so-called mediating factors might provide opportunities for prevention and intervention programs.

The objective of this thesis was to extend the existing knowledge on the relation of social disadvantage with pregnancy outcomes and behaviour early in life. Since the exact pathways how social disadvantage 'gets under the skin' and causes pregnancy complications and behavioural problems are partly unknown, we aimed to identify the mechanisms underlying these associations. The specific aims of this thesis were:

1a. To study the association between social disadvantage and pregnancy outcomes, of which preterm birth and birth weight were the main focus.
1b. To examine explanatory mechanisms in educational and employment-related inequalities in adverse pregnancy outcomes.

2a. To study the association of social disadvantage with child behaviour and parental harsh discipline in early childhood.
2b. To examine explanatory mechanisms in socioeconomic and ethnic inequalities in child behaviour and parental harsh discipline.

The studies described in this thesis were embedded in The Generation R Study, which is a prospective population-based cohort study from fetal life onwards in Rotterdam, the Netherlands.

In *chapter 2* of this thesis, we studied the association between social disadvantage and different pregnancy outcomes. *Chapter 2.1* described that low maternal educational level, as an indicator of low SES, was associated with slower fetal growth resulting in differences in fetal weight. The adverse effect of low education was largest for growth of the fetal head, followed by growth of the fetal femur and abdomen. The educational inequalities in fetal growth characteristics were largely due to determinants of fetal growth, such as maternal smoking during pregnancy and maternal height. The inequalities in fetal head circumference, however, remained partly unexplained.

In *chapter 2.2*, we showed that pregnant women with a low educational level had a nearly two-fold higher risk of preterm birth as compared to women with a high educational level. A combination of several risk factors for preterm birth among women with a low education, namely pre-eclampsia, intrauterine growth retardation, mothers' young age, short stature and high body mass index, smoking habits, financial concerns, and indicators of poor psychosocial functioning, explained this elevated risk. Moreover, low educated women were more likely to abstain from drinking alcohol during pregnancy, which also contributed to their increased risk of preterm birth. We hypothesized that low to moderate alcohol consumption during pregnancy may be genuinely beneficial in preventing preterm birth, but the effects may also be explained by the 'healthy drinker effect'. This phenomenon implies that women with a poor obstetric history are more likely to abstain from drinking during pregnancy.

Chapter 2.3 indicated that offspring's birth weight was on average 176 grams lower among the lowest educated women as compared to high educated women. A substantial part of this lower birth weight was the result of a shortened gestational period among women with a low educational level. The remaining birth weight difference of 126 grams between low and high education was partially due to an accumulation of risk factors for low birth weight among low educated women, namely: parental height and birth weight, hypertension, maternal age, parity, single motherhood, unplanned pregnancy, financial difficulties, number of people living in the household, weight gain, and most importantly maternal smoking during pregnancy. Despite the contribution of these mediating variables, part of the relationship between educational level and birth weight remained unexplained. Next to this, we also showed that, besides a relatively high prevalence of certain risk factors for low birth weight, lower educated women also have a relatively high prevalence of certain factors that have a suppressive effect on low birth weight. The suppressing variables were body mass index and weekly working hours.

Another indicator of social disadvantage included in this thesis was employment status. In *chapter 2.4*, we showed that unemployment among pregnant women, as compared to being employed, was associated with a higher risk of several adverse pregnancy outcomes, specifically preterm ruptured membranes, preterm birth, meconium stained amniotic fluid and small-for-gestational-age. These risks were entirely attributable to the less optimal socio-economic circumstances and poorer mental health of unemployed women. In contrast, unemployed women had a *lower* risk of a complicated delivery, i.e. poor progress of delivery and non-vaginal delivery, than employed women. The reason for this was that the unemployed women in our study were more often multiparous than unemployed women. In-depth analysis of the unemployed group revealed that women receiving disability benefit had the highest risk of several pregnancy complications. Among those with paid employment, we observed that long weekly working hours during pregnancy were significantly associated with a lower birth weight in the offspring. Weekly working hours were not associated with other pregnancy outcomes under study.

The second part of this thesis provides information on the association of social disadvantage with child behaviour and parental harsh discipline early in life. In *chapter 3.1* we showed that several indicators of low SES, such as low parental educational level, low family income and low maternal occupational level, were associated with a more difficult temperament in six months old infants as compared to indicators of high SES. Only the direction of the association between SES and Sadness was reversed. The effect of SES on the temperamental scales Distress to Limitations, Recovery from Distress, and Duration of Orienting was largely attributable to a young maternal age, single motherhood, family stress and poor maternal psychological well being. These covariates could not explicate the higher levels of Activity and Fear nor the lower Sadness scores of infants from low SES groups.

Chapter 3.2 described higher levels of parent-reported behavioural problems in toddlers from various backgrounds as compared to native Dutch children. This association was partly mediated by maternal psychopathology and indicators of SES. Besides this, we showed that the reported behavioural problems of non-Dutch children were more pronounced among those with unfavourable immigration characteristics of the mothers, such as being first generation immigrant, older than 15 years at immigration, having poor Dutch language skills and lack of feelings of acceptance by Dutch natives.

Finally, in *chapter 3.3*, we aimed to identify determinants of harsh discipline used by mothers and fathers of 3-year old toddlers. We demonstrated that psychosocial characteristics of parents, such as psychopathology and stress, were risk factors for use of harsh discipline by both mothers and fathers. Moreover, sociodemographic characteristics like young parental age and being first generation non-Western immigrant consistently predicted maternal and paternal harsh discipline. Indicators of socioeconomic status, however, were clearly associated with maternal harsh discipline, but hardly with paternal harsh discipline. A substantial part of the association between educational level and maternal harsh discipline was due to other sociodemographic characteristics such as ethnicity, family income, and young maternal age.

In *chapter 4* we considered our main findings regarding the mechanisms underlying the association of social disadvantage gradient with pregnancy complications and behaviour early in life. Next, we hypothesized about which factors might mediate the remaining social inequalities in pregnancy outcomes and child behaviour that could not be explained by the mediators we studied. We also discussed relevant methodological issues that possibly have influenced our findings. The last part of this chapter outlined some implications for public health policies.

SAMENVATTING

De sociale positie van individuen in een maatschappij is geassocieerd met gezondheid en ziekte, waarbij sociaal minder begunstigde personen het slechtst af zijn. De preventie van deze ongelijkheden in gezondheid is een belangrijk volksgezondheidsdoel. Aangezien gezondheidsverschillen tussen sociaal bevoordeelde en minder bevoordeelde personen al vroeg in het leven aanwezig zijn en volharden tijdens de gehele levensduur, zouden pogingen om deze verschillen aan te pakken moeten beginnen met het verminderen van sociaal-economische en etnische ongelijkheden in het foetale leven en de vroege kindertijd. De indicatoren van een lage sociale positie, zoals lage sociaal-economische positie en het behoren tot etnische minderheidsgroepen, zijn echter niet gemakkelijk te veranderen. Daarom is het belangrijk om de onderliggende mechanismen waardoor sociaal nadeel de gezondheid beïnvloedt te achterhalen, omdat deze zogenaamde mediërende factoren mogelijkheden voor preventie- en interventieprogramma's zouden kunnen bieden.

Het doel van dit proefschrift was de bestaande kennis over de relatie van sociale positie met zwangerschapsuitkomsten en gedrag in het vroege leven uit te breiden. Omdat deels onbekend is hoe sociale ongelijkheid 'onder de huid kruipt' en daarmee zwangerschapscomplicaties en gedragsproblemen veroorzaakt, hebben we geprobeerd de mechanismen die ten grondslag liggen aan deze relaties te identificeren. De specifieke doelstellingen van dit proefschrift waren:

1a. De associatie tussen sociale positie en zwangerschapsuitkomsten te bestuderen, waarbij de nadruk lag op de zwangerschapsuitkomsten, vroeggeboorte en geboortegewicht.
1b. De verklarende mechanismen in opleidings- en werkgerelateerde ongelijkheden in zwangerschapsuitkomsten te onderzoeken.

2a. De associatie tussen sociale positie enerzijds en gedrag van kinderen en een hardhandige opvoedingsstijl van ouders anderzijds te bestuderen.
2b. De verklarende mechanismen in etnische en sociaal-economische ongelijkheden in gedrag van kinderen en in een hardhandige opvoedingsstijl van ouders te onderzoeken.

De studies beschreven in dit proefschrift maken deel uit van de Generation R Studie, een prospectieve, populatie-gebaseerde cohortstudie vanaf het foetale leven in Rotterdam, Nederland.

In *hoofdstuk 2* van dit proefschrift bestudeerden wij de associatie tussen sociale positie en verschillende zwangerschapsuitkomsten. *Hoofdstuk 2.1* beschrijft dat een laag opleidingsniveau van zwangere vrouwen – als indicator van een lage sociaal – economische positie-geassocieerd was met een langzamere foetale groei, hetgeen resulteerde in verschillen in foetaal gewicht. Het ongunstige effect van laag

opleidingsniveau was het grootst voor de foetale groei van het hoofd, gevolgd door de foetale groei van het dijbeen en de buik. De opleidingsongelijkheden in foetale groeikenmerken waren grotendeels toe te schrijven aan determinanten van foetale groei, zoals lengte van moeder en roken tijdens zwangerschap. De ongelijkheden in foetale hoofdomtrek bleven echter gedeeltelijk onverklaard.

In *hoofdstuk 2.2* toonden wij aan dat zwangere vrouwen met een laag opleidingsniveau een bijna tweemaal zo hoog risico op een vroeggeboorte hadden in vergelijking met vrouwen met een hoog opleidingsniveau. Dit verhoogde risico werd verklaard door de aanwezigheid van verschillende risicofactoren voor vroeggeboorte onder vrouwen met een laag opleidingsniveau, namelijk pre-eclampsie, intrauterine groeivertraging, jonge leeftijd moeder, korte lengte en hoge body mass index van moeder, roken tijdens de zwangerschap, financiële zorgen en indicatoren van een slecht psychosociaal functioneren van moeder. Daarnaast drinken laag opgeleide vrouwen minder of geen alcohol tijdens zwangerschap; ook dit droeg bij aan hun verhoogde risico op een vroeggeboorte. Wij hypothetiseerden dat een matige alcoholconsumptie tijdens de zwangerschap daadwerkelijk een beschermende factor voor vroeggeboorte zou kunnen zijn. Anderzijds zou het 'healthy drinkereffect' ook een rol kunnen spelen; dit fenomeen impliceert dat vrouwen met een ongunstige obstetrische voorgeschiedenis zich eerder onthouden van het drinken van alcoholische consumpties tijdens de zwangerschap.

Hoofdstuk 2.3 wees uit dat het geboortegewicht van nakomelingen gemiddeld 176 gram lager was onder de laagst opgeleide vrouwen in vergelijking met de hoogst opgeleide vrouwen. Een groot deel van dit lagere geboortegewicht was het gevolg van een kortere zwangerschapsduur onder vrouwen met een laag opleidingsniveau. Het resterende verschil in geboortegewicht tussen baby's van laag en hoog opgeleide vrouwen (126 gram) was gedeeltelijk toe te schrijven aan een opeenhoping van risicofactoren voor een laag geboortegewicht onder laag opgeleide vrouwen, namelijk: lengte en geboortegewicht van de ouders, hypertensie, leeftijd van moeder, pariteit, alleenstaand moederschap, ongeplande zwangerschap, financiële moeilijkheden, aantal mensen in het huishouden, gewichtstoename tijdens de zwangerschap, en als belangrijkste factor, roken tijdens de zwangerschap. Ondanks de bijdrage van deze mediërende variabelen bleef een deel van het verband tussen opleidingsniveau en geboortegewicht onverklaard. Naast de opeenhoping van verschillende risicofactoren voor een laag geboortegewicht onder lager opgeleide vrouwen toonden wij ook aan dat deze vrouwen tevens enkele 'beschermende factoren' voor een laag geboortegewicht hadden. Lager opgeleide vrouwen hadden namelijk gemiddeld een hogere body mass index en een lager aantal werkuren per week dan hoger opgeleide vrouwen; deze factoren zijn gerelateerd aan een hoger geboortegewicht.

Werkloosheid is een andere indicator van lage sociale positie die we in dit proefschrift hebben bestudeerd. *Hoofdstuk 2.4* laat zien dat werkloosheid onder zwangere vrouwen, in vergelijking met het hebben van een betaalde baan, geassocieerd was met een hoger risico op verschillende ongunstige zwangerschapsuitkomsten, te weten vroegtijdig gebroken vliezen, vroeggeboorte, meconiumhoudend vruchtwa-

ter en foetale groeivertraging. Deze risico's waren volledig toe te schrijven aan de minder optimale sociaal-economische omstandigheden en de minder goede geestelijke gezondheid van werkloze vrouwen. In vergelijking met werkende vrouwen hadden werkloze vrouwen echter een minder grote kans op complicaties tijdens de bevalling, zoals een niet-vorderende ontsluiting of uitdrijving of een kunstverlossing. De verklaring hiervoor was dat de werkloze vrouwen in onze studie vaker al eerder een kind hadden gebaard dan werkende vrouwen. Analyses binnen de groep werkloze vrouwen liet zien dat arbeidsongeschikte vrouwen, in vergelijking met huisvrouwen, werkzoekenden en studenten, het hoogste risico hadden op zwangerschapscomplicaties. Onder zwangere vrouwen met een betaalde baan was fulltime werken (40 of meer uur per week), in vergelijking met parttime werken, geassocieerd met een lager geboortegewicht in de nakomelingen. In onze studie was aantal wekelijkse werkuren niet geassocieerd met andere zwangerschapsuitkomsten.

Het tweede deel van dit proefschrift betreft de associatie tussen sociale positie enerzijds en gedrag van jonge kinderen en een hardhandige opvoedingsstijl van ouders anderzijds. In *hoofdstuk 3.1* toonden wij aan dat verschillende indicatoren van een lage sociaal-economische positie, zoals laag opleidingsniveau van ouders, laag gezinsinkomen en laag beroepsniveau van moeder, geassocieerd waren met een moeilijker temperament in zes maanden oude baby's. Alleen de richting van het verband tussen sociaal-economische positie en de temperamentschaal Sadness was omgekeerd. Het effect van sociaal-economische positie op de temperamentschalen Distress to Limitations, Recovery from Distress, en Duration of Orienting was grotendeels toe te schrijven aan een jonge leeftijd van moeder, alleenstaand moederschap, stress binnen het gezin en psychische problemen van moeder. Deze variabelen konden de hogere scores op de temperamentschalen Activity en Fear en de lagere scores op Sadness van baby's afkomstig uit gezinnen met een lagere sociaal-economische positie niet verklaren.

Hoofdstuk 3.2 beschrijft dat immigranten ouders met een niet-Nederlandse achtergrond meer gedragsproblemen bij hun peuters rapporteren dan Nederlandse ouders. Deze associatie werd gedeeltelijk verklaard door een lage sociaal-economische positie en door psychopathologie van de moeder. Hiernaast toonden wij aan dat de gedragsproblemen van niet-Nederlandse kinderen groter waren als er sprake was van ongunstige immigratiekenmerken bij de moeders, zoals eerste generatie immigrant zijn, ouder dan 16 jaar zijn ten tijde van de immigratie, slechte Nederlandse taalvaardigheden hebben en het gevoel hebben niet geaccepteerd te worden door Nederlanders.

Tot slot was het doel in *hoofdstuk 3.3* om determinanten van het gebruik van een hardhandige opvoedingsstijl te identificeren. Hiertoe bestudeerden we de opvoedingsstijl van moeders en vaders van 3-jaar oude kinderen. Wij toonden aan dat psychosociale kenmerken van ouders, zoals psychopathologie en het ervaren van stress, voorspellers zijn voor het hanteren van een hardhandige opvoedingsstijl bij zowel moeders als vaders. Tevens waren sociodemografische kenmerken, zoals

jonge leeftijd van de ouders en een niet-Westerse achtergrond (alleen eerste generatie immigranten), voorspellers voor een hardhandige opvoedingsstijl van beide ouders. De indicatoren van sociaal-economische positie waren echter duidelijk geassocieerd met het gebruik van een hardhandige opvoedingsstijl van moeders, maar nauwelijks met het hanteren van een hardhandige opvoedingsstijl door vaders. De bevinding dat laag opgeleide moeders vaker een hardhandige opvoedingsstijl hanteren was deel toe te schrijven aan andere sociodemografische kenmerken, zoals een niet-Nederlandse achtergrond, laag gezinsinkomen en jonge leeftijd van moeder.

Hoofdstuk 4 geeft een meer algemene discussie van de belangrijkste bevindingen. Omdat we niet alle sociale ongelijkheden in zwangerschapsuitkomsten en gedrag van kinderen konden verklaren in dit proefschrift, hypothetiseerden we in dit hoofdstuk welke factoren verder een rol zouden kunnen spelen. Tevens worden enkele methodologische kwesties besproken die onze bevindingen mogelijk hebben beïnvloed. Het laatste deel van dit hoofdstuk beschrijft enkele implicaties voor het volksgezondheidsbeleid.

LIST OF ABBREVIATIONS

AC	Abdominal circumference
BMI	Body mass index
BM	Basic model
BSI	Brief Symptom Inventory
CI	Confidence interval
CBCL/1½ -5	Child Behavior Checklist for toddlers
CTQ	Childhood Trauma Questionnaire
CTS-PC	Parent-Child Conflict Tactics Scale
df	Degrees of freedom
FAD	Family Assessment Device
FL	Femur length
HC	Head circumference
IBQ-R	Infant Behaviour Questionnaire-Revised
IUGR	Intrauterine growth restriction
OR	Odds ratio
SD	Standard deviation
SES	Socioeconomic status
SGA	Small-for-gestational-age

DANKWOORD

Een proefschrift schrijven doe je natuurlijk niet alleen… Veel mensen hebben direct of indirect een bijdrage geleverd aan dit proefschrift. Het zijn te veel mensen zijn om allemaal persoonlijk te bedanken, maar een aantal wil hier toch graag noemen!

Bedankt…

… 9778 DEELNEMENDE MOEDERS, VADERS EN KINDEREN
Zonder jullie waren er geen gegevens geweest om over te schrijven. Bedankt voor het belangeloos invullen van (lange) vragenlijsten en het enthousiasme waarmee jullie meedoen aan Generation R.

… 2 PROMOTOREN
Prof.dr. Mackenbach en *prof.dr. Verhulst*, beste Johan en Frank, ik waardeer het erg dat jullie in je drukke agenda's altijd een gaatje vonden om mijn stukken te lezen en van scherp en helder commentaar te voorzien. Ik heb veel geleerd van jullie expertise en jarenlange onderzoekservaring.

… 2 CO-PROMOTOREN
Hein, bedankt voor je enthousiaste instelling! Je vond alle resultaten boeiend en zag veel mogelijkheden voor leuke artikelen; dit werkte aanstekelijk. We hebben samen veel gepuzzeld over statistische analyses en hoe we de resultaten het beste konden rapporteren. Maar we zijn er uit gekomen! Hopelijk werken we in de toekomst nog eens samen aan nieuwe projecten.
Henning, ik denk met plezier terug aan de nuttige en gezellige uurtjes op de Westzeedijk bij het bespreken van mijn werk. Ik heb veel van je kennis en denkwijze opgestoken. Je stond altijd klaar om me te helpen en dat waardeer ik zeer! Tevens wil ik je bedanken voor de kans die je me hebt gegeven om als postdoc onderzoeker aan de slag te gaan. Ik ben blij dat ik nog een tijdje onder jouw hoede verder mag werken!

… 6 COMMISSIELEDEN
Professor Moll, bedankt dat u de secretaris van mijn leescommissie wilde zijn.
Professor Power and *professor Vollebergh*, I would like to thank you for reading and evaluating my manuscript.
Professor Bonsel, *professor Hirasingh* en *professor Muris* wil ik bedanken voor het plaatsnemen in mijn commissie.

… 2 PROJECTLEIDERS
Rosalinde Snijders, helaas heb ik niet zo lang met je samengewerkt, maar de korte tijd heb ik wel als prettig ervaren! Bedankt voor je inzet bij het opstarten van Generation R!

Vincent Jaddoe, je deur (of email) staat altijd open voor de promovendi en dat is fijn te weten. Bedankt voor je heldere, snelle reacties en goede ideeën!

... 1 MENTAL FATHER

Professor Hofman, ik hoop niet dat u het erg vindt, maar ik zie u toch altijd een beetje als de 'mental father' van Generation R. Bedankt voor uw lessen in de epidemiologie en aanstekelijke enthousiasme!

... 15 CO-AUTEURS

Dr. M.J. Bakermans-Kranenburg, Lex Burdof, professor Van Ijzendoorn, Caspar Looman, Floor van Oort, professor Steegers en de anderen die elders in dit dankwoord worden genoemd: bedankt voor jullie hulp en waardevolle feedback op de artikelen!

... X MEDEWERKERS VAN ZIEKENHUIZEN, VERLOSKUNDIGE PRAKTIJKEN, STAR-MDC, DE CB'S EN DE GGD

Dank voor jullie inzet bij het rekruteren van alle deelnemers en jullie bijdrage aan het verzamelen van gegevens van die bijna 10.000 deelnemers!

... X BUREAU-MEDEWERKERS, ONDERZOEKSASSISTENTEN, FOCUSMEDEWERKERS EN HUISBEZOEKERS

Bedankt voor jullie enthousiaste en kundige bijdrage aan Generation R en alle ondersteuning! Een speciaal woordje van dank aan *Patricia, Claudia* en *Elise* bij wie ik regelmatig binnenliep met vragen of voor advies. Jullie stonden altijd klaar om me te helpen, super!

... 45 COLLEGA-PROMOVENDI BIJ GENERATION R

Hanan, Tamara, Jens, Lindsay, Lenie, Noor, Fleur, Sarah, Dennis, Miranda, Sabine, Bero, Joost, Rachel en alle anderen: bedankt voor de fijne samenwerking, maar vooral ook voor alle gezelligheid! De borrels, uitjes, etentjes, dinsdag- en donderdagkoffie, congresbezoeken en skivakanties gaven wel een extra dimensie aan het werken bij Generation R!
Een speciale dank voor *Lindsay,* mijn roomy: ruim drie jaar hebben we samen kamertje AE-003 bewoond. Wat hebben we veel gedeeld en geploeterd met z'n tweeën! Bedankt voor je hulp, gezelligheid en alle snacks die in de loop van middag uit je tas tevoorschijn kwamen. Het was fijn om een kamer met je te delen!
En natuurlijk ook een speciale dank voor *Miranda*, collega maar inmiddels ook vriendin! Dank je wel dat je me bij wilt staan op 4 december!

... 25 COLLEGA'S VAN HET KSCD VAN BUREAU JEUGDZORG

Anneke, Madelon, Esther, Jan, Marianne en alle anderen: bedankt voor jullie belangstelling in mijn onderzoek, fijne gesprekken, de geboden mogelijkheden en de prettige samenwerking!

... 1 GRAFISCH ONTWERPER
Jan, wat is het een mooi boekje geworden! Bedankt voor al je moeite en de gezellige werkoverleggen!

... EEN HOOP VRIENDEN
Lieve *Lies, Iris, An, Cin*, lieve *Al Dentes* en lieve *andere vrienden en vriendinnen*! Jullie hebben voor de broodnodige afleiding en ontspanning gezorgd! Bedankt allemaal voor jullie vriendschap; het is fijn om lief en leed met jullie te delen!

... 6 VERBURGJES
Lieve *Brigit, Arjen, Heske, Lennart, Benten en Feija*, ik voel me erg welkom bij jullie en had me geen fijnere schoonfamilie kunnen wensen! Bedankt voor jullie interesse en optimistische inslag!

... 6 JANSENTJES
Lieve *papa en mama*, jullie wisten al veel eerder dan ikzelf dat promoveren wel wat voor mij was. Wat kennen jullie me toch goed! Bedankt dat jullie altijd voor me klaar staan en voor alle liefde die jullie me geven!
Lieve *Wouter en Sabine*, wat een avondje voetbal kijken al niet te weeg kan brengen! Ik ben blij dat jullie elkaar gevonden hebben! Bedankt voor jullie liefde, vriendschap en mijn twee stoere neefjes! *Sabine*, ik ben blij dat je naast me staat tijdens mijn verdediging!

…
Bero, mijn lieve Bo! Het is bijna niet mogelijk om je te bedanken voor alles wat je voor me betekent. Ik ben blij dat ik je ben tegengekomen, want het leven met jou samen is een feestje! Bedankt voor alles, je liefde en je heerlijke levensmotto: "*Go with the flow*"!

ABOUT THE AUTHOR

Pauline Jansen was born in Vlissingen, the Netherlands, on June 2nd, 1980. She passed secondary school in 1998 at S.S.G. Scheldemond in Vlissingen and started studying Psychology at the University of Leiden. She had her internship at the Department of Child and Adolescent Psychiatry in the Sophia's Children's Hospital, Erasmus Medical Center. Next, she participated in a research project on behavioural problems in children with 22q11 deletion syndrome at the Department of Medical Psychology at the Wilhelmina Children's Hospital, University Medical Center Utrecht. In Januari 2004, she graduated in Developmental & Educational Psychology and in Clinical & Health Psychology. In the autumn of the same year, she started at the Erasmus Medical Center with the research project presented in this thesis. The project was a collaboration of the Department of Child and Adolescent Psychiatry and the Department of Public Health. She obtained a Master of Science degree in Epidemiology from the Netherlands Institute for Health Sciences (Nihes) in 2007. From January 2008 onwards, she also worked part-time as a psychologist at Bureau Jeugdzorg Stadsregio Rotterdam. In December 2008, the Sophia Foundation for Scientific Research granted her research proposal "*Harassment in kindergarten: Who bullies, and why?*" In July 2009, she started this post-doctoral fellowship at the Department of Child and Adolescent Psychiatry in the Sophia's Children's Hospital, Erasmus Medical Center. She combines this function with a position at Bureau Jeugdzorg Stadsregio Rotterdam, where she is involved in research activities within this organization.

PHD PORTFOLIO

NAME PHD STUDENT: P. W. Jansen
ERASMUS MC DEPARTMENTS:
Child and Adolescent Psychiatry
Public Health
RESEARCH SCHOOL: NIHES

PHD PERIOD: October 2004 – May 2009
PROMOTORS:
J.P. Mackenbach and F.C. Verhulst
SUPERVISORS:
H. Raat and H. Tiemeier

1. PhD training

	Year	Workload (ECTS)
Research skills		
NIHES courses:		
Principles of Research in Medicine and Epidemiology	2005	0.7
Methods of Public Health Research	2005	0.7
Health Economics	2005	0.7
Topics in Evidence-based Medicine	2005	0.7
Cohort Studies	2005	0.7
Introduction to Public Health in the Changing Global Context	2005	0.7
Public Health Research: Analysis of Population Health	2005	1.4
Public Health Research: Analysis of Determinants	2005	1.4
Public Health Research: Intervention Development and Evaluation	2005	1.4
Study design	2006	3.0
Classical Methods for Data-analysis	2006	5.7
Methodological Topics in Epidemiologic Research	2006	1.4
Modern Statistical Methods	2006	4.3
In-depth courses		
Repeated measurements in clinical studies, NIHES	2006	1.4
Missing values in clinical research, NIHES	2006	1.4
Public Health in the European Union, NSPOH	2006	1.4
Addiction and substance use, NIHES	2006	1.4
(Inter)national conferences – participation and presentations		
DOHaD 2005, 3rd International Congress on Developmental Origins of Health & Disease, Toronto, Canada. Poster presentation: *Socioeconomic Differences in Birth Weight and in Maternal Life Style Determinants of Birth Weight*.	2005	1.4
IFPE 2007, 11th Congress of the International Federation of Psychiatric Epidemiology, Göteborg, Sweden. Poster presentation: *Observed maternal sensitivity and infant temperament. The Generation R Study*.	2007	1.4
Projectleidersbijeenkomst GeestKracht en LAK GGz/Vz, Nieuwegein, the Netherlands. Poster presentation: *Observed maternal sensitivity and infant temperament.*	2007	0.5
Nederlands Congres voor Volksgezondheid 2008, Groningen, the Netherlands. Oral presentation: *Sociaal-economische status en zwangerschapsuitkomsten: welke factoren dragen bij aan de ongelijkheden?*	2008	0.9
Voorjaarscongres van de Nederlandse Vereniging voor Psychiatrie, Amsterdam, the Netherlands. Oral presentation: *Sociaal-economische status en gedragsproblemen bij 1½ jaar oude kinderen.*	2008	0.9
IACAPAP, 18th World Congress of the International Association for Child and Adolescent Psychiatry and Allied Professions. Istanbul, Turkey. Oral presentation: *Socioeconomic Status and Behavioral Problems in 1½-year-old toddlers.*	2008	1.4
IFPE 2009, 12th Congress of the International Federation of Psychiatric Epidemiology. Vienna, Austria. Oral presentation: *National origin and behaviour problems of toddlers: the role of maternal familial adversities and migration characteristics.*	2009	1.4
Seminars and workshops		
Seminar over wetenschappelijk publiceren, afdeling Maatschappelijke gezondheidszorg, Erasmus MC Rotterdam	2004	0.3
Minicursus Methodologie van patiëntgebonden onderzoek en voorbereiding van subsidieaanvragen, Erasmus MC Rotterdam	2006	0.3

PHD PORTFOLIO (CONTINUED)

2. Teaching activities	Year	Workload (ECTS)
Supervising practicals and excursions		
Supervising practicals Child and Adolescent Psychiatry for medical students	2008	0.6
Supervising Master's theses		
Supervised Esther Neidt, student Developmental & Educational Psychology, Erasmus University Rotterdam. Thesis title: *The association between maternal employment and child behaviour.*	2008	2.0
Supervised Evelien Blom, medical student, Erasmus MC-University Medical Center Rotterdam. Thesis title: *Perinatal complications increase the risk of postpartum depression. The Generation R Study.*	2008	2.0