



**Karolinska
Institutet**

**Institutionen för klinisk forskning och utbildning,
Södersjukhuset**

Long-term Consequences of Preterm Birth: Swedish National Cohort Studies

AKADEMISK AVHANDLING

som för avläggande av medicine doktorexamen vid Karolinska Institutet
offentligen försvaras på svenska språket i sal Ihre, Södersjukhuset, plan 0.

Tisdagen den 31 maj 2011, kl. 09.00

av

Karolina Lindström
Leg. läkare

Huvudhandledare:

Adjungerad professor Anders Hjern, Nordiska
Högskolan för folkhälsovetenskap, och
Centre for Health Equity Studies, Karolinska
Institutet/Stockholms Universitet

Bihandledare:

Med. dr. Ihsan Sarman
Karolinska Institutet
Institutionen för klinisk forskning och utbildning

Bihandledare:

Professor emeritus Birger Winblad
Karolinska Institutet
Institutionen för klinisk forskning och utbildning

Fakultetsopponent:

Professor emeritus Orvar Finnström
Linköpings Universitet
Institutionen för klinisk och experimentell
medicin, Linköping

Betygsnämnd:

Docent Josef Milerad
Karolinska Institutet
Institutionen för kvinnors och barns hälsa

Docent Gunilla Malm

Karolinska Institutet
Institutionen för klinisk vetenskap, intervention
och teknik (CLINTEC)

Professor Uwe Ewald

Uppsala Universitet
Institutionen för kvinnors och barns hälsa

Stockholm 2011

ABSTRACT

The World Health Organization defines preterm birth as birth before 37 complete weeks. The proportion of *very* preterm children with severe neurological disabilities has become smaller, but bulks of data indicate that, for many of the children born preterm, persistent subtle difficulties are evident in school age. Most studies have focused on the situation for infants born before 33 complete weeks. However, *moderately* preterm (gestational week 33–36) are much more common, and hence important from a public health perspective. In this thesis, long-term consequences of all degrees of preterm birth in school age and young adulthood have been studied. Swedish national registers have been used as data sources. The outcomes for preterm individuals have been compared with the outcomes for infants born at term (here defined as 39–41 gestational weeks).

The objective was to investigate the impact of preterm birth on social adjustment, mental health and asthma. Also, the interplay between preterm birth and socioeconomic characteristics of the childhood household has been analysed. One cohort of over half a million individuals born 1973–79 and another cohort of over a million individuals born 1987–2000 have been used for these purposes.

The risk for inhaled corticosteroid medication (our main indicator for asthma) in 6–19 year-olds born 1987–2000 increased with the degree of prematurity. For prematurely born children, compared with children with similar socioeconomic backgrounds born at term, the risk increased from 10 % in 37–38 weeks of gestation at birth, to more than a doubled risk for 23–28 weeks of gestation.

For individuals born 1987–2000, there was a stepwise increase in odds ratios for Attention-Deficit/Hyperactivity Disorder medication (our indicator for ADHD) at 6–19 years of age, with increasing degree of immaturity at birth from more than a doubled risk for infants born after 23–28 weeks of gestation, to a 20 % increased risk for 37–38 weeks of gestation compared with infants born after 39–41 weeks and with adjustment for socioeconomic confounders. Furthermore, individuals born 1973–79 were followed-up at 8–29 years of age for psychiatric hospital admissions. Compared with term infants the increase of risk varied by increasing maturity at birth, from just below 70 % for gestational week 24–32 down to just below 10 % for gestational week 37–38, with adjustment for socioeconomic confounders.

The large majority of even the most preterm (< 29 gestational weeks) born in 1973–79 led productive and independent lives in young adulthood. Very preterm individuals (< 33 gestational weeks), however, ran almost four times the risk for disability, after adjustment for socioeconomic and perinatal indicators compared with term individuals (39–41 weeks). The increased risk for disability dropped gradually with higher gestational age at birth, but was still significantly increased for gestational week 37–38 compared with gestational week 39–41.

Moderately preterm individuals to mothers of low education were more sensitive to the effect of preterm birth on the risk for ADHD. Accordingly, children growing up in socially disadvantaged households, as expressed by low socioeconomic status, were more vulnerable to the effect of preterm birth on psychiatric morbidity.

Conclusions

The risks for the unfavorable outcomes studied increased with decreasing gestational age at birth in the follow-up studies of individuals born 1973–79 and 1987–2000. The most preterm group (< 33 complete weeks) born in the seventies contributed more economically to society than they received in societal assistance/benefits. Moderately preterm and early term carried, due to their large number, most of the morbidity associated with preterm/early term birth. Hence, this group is important from a public health perspective and deserves more attention in research and clinical development.