



**Karolinska
Institutet**

Institutionen för Medicinsk Epidemiologi och Biostatistik

Prenatal influences on health outcomes over the lifespan

Effects of smoking, socio-economic status and foetal growth

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Karolinska
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av

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ABSTRACT

The most remarkable development during a person's life takes place in utero. Through about 280 days of proliferation and differentiation one single cell is developed into a human being. As this is the time when the whole body is formed, it is easy to imagine that exposures during this time can have health consequences over the lifespan. Indeed, a large number of studies have shown that early exposures, such as low birth weight and maternal smoking during pregnancy, influence health later in life, for example the risks of hypertension and cardiovascular disease. However, it has been questioned if the found associations really reflect causal relationships, or if they are due to genetic or environmental confounders. The aim of this thesis was to study how factors during prenatal/early life can influence health outcomes over the lifespan, after taking common genetic and shared environmental factors into account. The focus lies on intergenerational influences of smoking, socio-economic status and foetal growth.

In the first study it is investigated if a change in maternal smoking habits between two consecutive pregnancies influences the risk of stillbirth. It was found that women who quit smoking between pregnancies have the same risk of stillbirth in their second pregnancy as women who never smoked when pregnant. Women, who smoked in one of their two pregnancies, had an increased risk of stillbirth in the pregnancy where they smoked compared to the pregnancy when they did not smoke. These findings support the conclusion of a causal association between maternal smoking during pregnancy and stillbirth.

In the second study it is investigated if maternal smoking during pregnancy has a long term influence on offspring blood pressure. A small but statistically significant increase in systolic and diastolic blood pressure was found in sons whose mothers had smoked during pregnancy. This association remained, although not statistically significant, within brother pairs. The conclusion is that there might be a long term influence of maternal smoking during pregnancy on offspring blood pressure.

In the third study it is investigated if intergenerational social mobility influences the risk of hypertension. The results showed a decreased risk of hypertension among twins with upward social mobility and indicated an increased risk among twins with downward social mobility. The conclusion is that social inequity in hypertension is initiated early in life (indicated by parental social status), but modifiable through later factors (indicated by adult social status).

In the fourth study it is investigated if the intergenerational influence on birth weight/birth length is due to genes or environment. An association between mother's and offspring's size at birth was found within birth weight discordant dizygotic twin pairs, but not within monozygotic twin pairs. The conclusion is that the intergenerational association in size at birth is due to direct or indirect genetic factors.