



## GRIP STRENGTH AT AGE 58 AFTER PRENATAL EXPOSURE TO THE DUTCH FAMINE

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**Abstract:** *Background:* Grip strength is a marker of current and future health. Small size at birth is associated with reduced grip strength and poor health in later life. Prenatal undernutrition may affect adult grip strength. We investigated the effect of prenatal undernutrition on grip strength in the Dutch famine birth cohort. *Methods:* We assessed grip strength in 334 men and 364 women at age 58, born as term singletons around the time of the 1944-45 Dutch famine. We compared grip strength among men and women who had been exposed to famine during different periods of gestation to unexposed subjects. *Results:* Men exposed to famine in early gestation had a 4.2 kg (95%CI 1.0 to 7.3) greater grip strength compared to unexposed men. After adjustment for adult height and timing of participation in the study, the association was no longer significant (2.9 kg (95%CI -0.2 to 6.0)). In women, prenatal exposure to famine was not significantly associated with grip strength. A 1 kilogram increase in birth weight was associated with an increase of 2.8 kg (95%CI 1.0 to 4.7) in grip strength in men and 1.5 kg (95%CI 0.1 to 2.8) in women, adjustment for adult body size explained this relationship. *Conclusions:* There was no evidence for significant independent associations between prenatal famine exposure and adult grip strength although men exposed in early gestation appeared to have increased grip strength explained by taller adult height. Consistent with previous studies, there was a relationship between small size at birth and lower grip strength.

**Key words:** Grip strength, famine, programming.

### Introduction

Handgrip strength can be used as a marker of overall muscle strength (1). Decreased grip strength is associated with the presence of chronic diseases including coronary heart disease, stroke, chronic obstructive pulmonary disease and diabetes mellitus (13). Grip strength is known to decline with age and poor grip strength is associated with increased all-cause mortality (2). Birth weight is positively associated with adult grip strength (6, 7), and therefore grip strength is thought to be affected by environmental influences in early life.

The Dutch famine was a period of severe food shortage in the west of the Netherlands that occurred during the last 5-6 months of World War II. The famine offers a unique opportunity to study the effects of prenatal

undernutrition on health in later life. Among several adverse health effects, people conceived during the famine had a more atherogenic lipid profile (17) and an earlier onset and a doubled rate of coronary artery disease (10). Also, people exposed to the famine during gestation had impaired glucose tolerance (4, 14). Recently, we demonstrated that people conceived during the famine performed worse on a selective attention test, a cognitive ability that is known to decline with age. This was the first evidence in the Dutch famine birth cohort that suggests that prenatal undernutrition is associated with accelerated aging (5).

In the present study, we investigated grip strength in men and women born around the time of the Dutch famine, aged 56-61 years. We hypothesized that people who were prenatally exposed to famine would have reduced grip strength at adult age.

### Methods

#### *The Dutch famine birth cohort*

The Dutch famine birth cohort members were born as term singletons between 1 November 1943 and 28

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February 1947 in the Wilhelmina Gasthuis in Amsterdam, the Netherlands. The selection procedures for this cohort have been described elsewhere (14). At age 58, 1423 of the 2414 original cohort members (58%) were still alive, living in the Netherlands and their address was known to the investigators. These people were eligible for our study. Of the group of 1423 eligible people, 810 (57%) agreed to participate at age 58 years. All participants gave written informed consent.

### *Exposure to famine*

Exposure to famine was defined according to the official daily food-rations for the general population older than 21 years. The official rations accurately reflect the variation over time in the total amount of food available in the west of the Netherlands (21). We considered fetuses to have been exposed to famine in utero if the average daily rations during any 13-week period of gestation were less than 1000 calories. Therefore, people born between 7 January 1945 and 8 December 1945 were considered to be exposed to famine in utero. We defined periods of 16 weeks each to differentiate between those who were exposed to famine in late gestation (born between 7 January 1945 and 28 April 1945), in mid gestation (born between 29 April 1945 and 18 August 1945) and in early gestation (born between 19 August 1945 and 8 December 1945). People born before 7 January 1945 (and were thus born before the famine) and those born after 8 December 1945 (and who had thus been conceived after the famine) were considered to be unexposed to famine in utero.

### *Study parameters*

The medical birth records provided information about the mother, the course of the pregnancy and the size of the baby at birth (14). Between September 2002 and October 2004 at a mean age of 58.3 (SD 0.9) years participants visited the clinic where trained study nurses carried out all measurements. As a marker of muscle strength, maximum grip strength was measured using a Jamar handgrip dynamometer (PGB, Bussum, The Netherlands) at the clinic visit. Grip strength was measured three times on each side, and the maximum of these measurements was used for the analyses. We measured height using a fixed or a portable stadiometer and weight using Seca scales or portable Tefal scales.

### *Statistical analyses*

We used linear regression analyses to compare the characteristics of individuals exposed in late mid or early gestation with characteristics of those who had not been exposed to famine in gestation. Linear regression was also performed to explore the association between

prenatal exposure to famine and maximum grip strength and between birth weight and maximum grip strength. Analyses were adjusted for current body size by adding height into the model. Further adjustments were made for the time at which the subjects participated during the study (date) since this contributed significantly to the variance in grip strength. In accordance with the existing literature, men and women were analyzed separately. We considered differences to be statistically significant if  $p < 0.05$ . Where  $p$ -values are given, they are 2 sided. We used SPSS 17.0 for all analyses.

## **Results**

Grip strength data were available for 334 men and 364 women who visited the hospital, after excluding participants ( $N=37$ ) with complaints of osteoarthritis, rheumatic disease and neurological and physical complaints that influenced the grip strength measurements. The birth weights of persons included in the study (3363 g) did not differ significantly from the birth weights of those not included in the study (3339 g;  $p=0.3$ ).

Table 1 shows the characteristics of the participants according to timing of exposure to famine in utero. One-hundred and twenty-nine (39%) men and one-hundred and fifty-nine (44%) women had been exposed to famine in utero. The control group consisted of individuals born before the famine and those conceived and born after the famine. These groups were comparable with respect to gestational age, birth weight, adult weight and height or maximum grip strength (all  $p > 0.05$ ). Male and female babies exposed to famine in late or mid gestation were lighter at birth than those not exposed. Gestational age was highest in men exposed to famine in early gestation. There was no significant difference in adult body size in exposed men and women compared to unexposed controls.

Table 2 shows the differences in hand grip strength according to timing of prenatal exposure to famine compared to non-exposed participants. Men exposed to famine in early gestation had greater hand grip strength than unexposed men (mean difference 4.2 kg (95%CI 1.0 to 7.3)). After adjustment for adult height and timing of participation in the study this association was no longer significant (2.9 kg (95%CI -0.2 to 6.0)). Prenatal famine exposure in mid or late gestation was not associated with hand grip strength in men. In women no association was found between prenatal exposure to famine and hand grip strength, neither in the unadjusted nor the adjusted analyses. Addition of birth weight or age to the linear regression models did not change the associations.

Considering the whole cohort irrespective of exposure status, both in men and women birth weight was strongly related with adult hand grip strength. An increase of 1 kilogram in birth weight was associated with an increase of 2.8 kg in hand grip strength (95% CI 1.0 to 4.7) in men



**Table 1**  
General, birth and adult characteristics according to timing of prenatal exposure to the Dutch famine, men and women separately

	Exposure to famine					all (SD)
	born before	in late gestation	in mid gestation	in early gestation	conceived after	
<b>MEN</b>						
N	106	56	43	30	99	334
gestational age (days)	283	282	286	291*	285	285 (12)
birth weight (kg)	3.42	3.25*	3.27*	3.51	3.57	3.43 (0.47)
weight (kg)	90.5	87.8	85.4	93.9	88.9	89.2 (15)
height (m)	1.77	1.77	1.76	1.79	1.77	1.77 (0.06)
maximum grip strength (kg)	50.3	50.3	49.7	55.0*	51.5	51.0 (8.4)
<b>WOMEN</b>						
N	107	67	59	33	98	364
gestational age (days)	285	283	285	287	285	285(11)
birth weight (kg)	3.37	3.16*	3.15*	3.41	3.41	3.31 (0.46)
weight (kg)	78.2	77.0	76.1	74.3	79.2	77.6 (14)
height (m)	1.65	1.64	1.64	1.64	1.64	1.64 (0.06)
maximum grip strength (kg)	29.3	30.0	29.0	30.0	28.9	29.3 (6.1)

\*p<0.05 for differences with born before and conceived after

**Table 2**

Differences (and 95% confidence intervals) in hand grip strength (kg) in men and women according to the timing of prenatal exposure to famine compared to non-exposed participants (those born before or conceived after the famine)

	Late gestation		Mid gestation		Early gestation	
	Men	Women	Men	Women	Men	Women
Unadjusted	-0.6 (-3.0 to 1.9)	1.0 (-0.7 to 2.7)	-1.2 (-3.9 to 1.6)	-0.1 (-1.9 to 1.7)	4.2 (1.0 to 7.3)*	0.9 (-1.3 to 3.2)
Adjusted for height	-0.6 (-3.0 to 1.7)	1.0 (-0.6 to 2.6)	-0.9 (-3.5 to 1.7)	0.1 (-1.6 to 1.8)	3.4 (0.4 to 6.5)*	1.0 (-1.2 to 3.1)
Height and time	-1.0 (-3.3 to 1.4)	0.7 (-0.9 to 2.3)	-1.2 (-3.8 to 1.4)	-0.0 (-1.7 to 1.6)	2.9 (-0.2 to 6.0)	1.0 (-1.2 to 3.1)

\*p<0.05

and 1.5 (95% CI 0.1 to 2.8) in women. After adjustment for age and adult height, this association was no longer significant. The association was largely explained by adult height (table 3).

**Table 3**

Differences (and 95% confidence intervals) in hand grip strength (kg) according to birth weight (kg) in the Dutch famine birth cohort (regardless of exposure status)

	Men	Women
Unadjusted	2.8 (1.0 to 4.7)*	1.5 (0.1 to 2.8)*
Adjusted for age	2.6 (0.7 to 4.5)*	1.4 (0.1 to 2.8)*
Adjusted for height	1.3 (-0.7 to 3.2)	0.1 (-1.3 to 1.5)
Age and height	0.9 (-1.0 to 2.9)	0.1 (-1.4 to 1.4)

\*p<0.05

## Discussion

In this study, we did not demonstrate any significant, independent associations between prenatal exposure to famine and adult grip strength. However men exposed to famine in early gestation appeared to have increased grip strength which was an unexpected finding. As reported

in previous studies, we found a positive relationship between size at birth and adult grip strength; however in this cohort of men and women, the association was largely explained by adult height.

The association between famine in early gestation and increased grip strength in men was surprising in view of earlier findings describing an increase in chronic disease among people exposed to famine in early gestation. It may represent a chance finding in the context of multiple comparisons, alternatively it may reflect bias in the study design or confounding. For example men exposed to famine in early gestation also tended to have a higher gestational age and to be younger as well as taller and heavier in adulthood. Certainly the association between famine in early gestation and increased grip strength in men was not independent of adult size and timing of participation in the study. However it is also possible that this was a true association perhaps mediated through increased muscle size. There is some evidence from studies in animal models that a period of reduced nutrition in early gestation can increase growth of tissues such as bone length possibly through an increase in IGF-1 level (9). However most animal studies focusing on skeletal muscle report that prenatal undernutrition is associated with reduced skeletal muscle fibre number or





density even in the absence of an effect on muscle weight (3, 12). Studies of the effect of early undernutrition on human muscle are sparse, however another natural 'experiment' found that children exposed to a period of undernutrition in late childhood were shorter and had higher appendicular lean mass/height<sup>2</sup> after the age of 65 years but there was no significant effect on grip strength (22).

The overall absence of significant, independent associations between prenatal exposure to famine and adult grip strength could be a true finding but alternative explanations also need to be considered. Selection bias is a common issue in cohort studies and some information bias may have existed in this round of data collection because the most frail individuals were seen at the end of the study for logistical reasons. To some extent this could be addressed by adjusting the findings for time seen. However allowing for the age of the participants was more problematic as the exposure variable and age were closely linked. However information bias with regard to the measurement of grip strength was likely to be minimal because we used a standardised grip strength measurement protocol (15). The age of our cohort was comparable to cohorts reporting the relationship between birth weight and adult grip strength (Hertfordshire Cohort Study, 59-73 years (20) and a British Cohort Study, 53 years (7, 8)). Lack of power is another possible explanation for our lack of associations. Although almost 700 people participated in the study, there were only 30 men exposed to famine in early gestation. These men also had greater adult height and weight, although the difference was not significant. Our study size is smaller than the other cohorts reporting on the association between birth weight and adult grip strength (6-8, 16, 18). Our findings therefore need replication in future studies.

Regardless of prenatal famine exposure we also found, as many other studies have done, that birth weight was positively associated with adult grip strength, the association being stronger for men than for women (6-8, 16, 18, 19). The magnitude of our findings was comparable to the findings of these earlier studies. Attenuation of the relationship between birth weight and grip strength after adjustment for adult size has been described previously (6, 7) and was demonstrated in our study with loss of the significant association after adjustment for height. One explanation is that adjusting for adult size using height, also corrects for muscle size which potentially lies on the causal pathway between low birth weight and reduced adult grip strength. The number of human skeletal muscle fibres is fixed by birth and there is preliminary evidence that low birth weight is associated with reduced myofibre score in later life (11).

In summary, there was no evidence for significant independent associations between prenatal exposure to famine and adult grip strength in this cohort although men exposed in early gestation appeared to have increased grip strength explained by adult taller height.

Consistent with previous studies, there was a relationship between small size at birth and lower adult grip strength.

### Key points

- Prenatal exposure to famine in early gestation was associated with greater grip strength in men; adjustment for adult size diminished this association.
- In women, we found no evidence that grip strength was influenced by prenatal exposure to famine.
- Grip strength was positively associated with size at birth; however adult size also explained this relationship.

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