

Early life factors associated with spirometric restriction in adulthood

Poor growth and nutritional deficits in utero and in childhood are associated with spirometric restriction in adult life, a longitudinal, multicohort population-based study has shown.

Data were analysed from three cohort studies, the Tucson Children's Respiratory Study (TCRS), in the USA, the Swedish Child (Barn), Allergy, Milieu, Stockholm, Epidemiological survey (BAMSE), and the Manchester Asthma and Allergy Study (MAAS) from the UK.

All three studies were designed to follow respiratory outcomes from birth.

The TCRS recruited 1,246 healthy infants at birth between April 1980 and October 1984.

Participants were followed up to age 36 and had regular spirometry (at age 22, 26, 32 and 36 years) with pre- and post-bronchodilator testing.

At each survey, participants were divided into one of three mutually exclusive groups:

- Normal ($FEV_1/FVC \geq 10$ th percentile and $FVC \geq 10$ th percentile)
- Restrictive ($FEV_1/FVC \geq 10$ th percentile and $FVC < 10$ th percentile)
- Obstructive ($FEV_1/FVC < 10$ th percentile, independent of FVC values)

In the TCRS cohort parental demographic data were collected during pregnancy and shortly after the birth together with information on respiratory history, nutritional status, smoking and education.

Participants' gestational age and weight were noted at birth and

growth monitored throughout the study. Surveillance for an asthma diagnosis was maintained throughout. Smoking was assessed by questionnaire from the age of 16.

Data collection for the other two cohorts was similar but did not include nutritional status during pregnancy.

In addition, total lung capacity was measured by body plethysmography in a random sample of 173 TCRS participants at the age of 32 years and in 407 MAAS participants at the age of 18 years.

Data on 652 participants in the TCRS who had at least one set of spirometry data contributing up to 1,668 observations were analysed.

Multivariate regression analysis showed that maternal nutritional problems during pregnancy; being born small for gestational age (birthweight < 10 th percentile) and being underweight in childhood (BMI for age < 5 th percentile) were independent predictors of spirometric restriction in adult life. Relative risk ratios (RRR) were as follows:

- **Maternal nutritional problems during pregnancy:** RRR 2.48 (95% CI: 1.30-4.76; $P = 0.0062$)
- **Small for gestational age:** RRR 3.26 (95% CI: 1.34-7.93; $P = 0.0093$)
- **Underweight in childhood:** RRR 3.54 (95% CI: 1.35-9.26; $P = 0.010$)

These risk factors were tested for replication in the BAMSE ($n = 1,817$) and MAAS ($n = 407$) cohorts. Associations between being born small for gestational age and being underweight in childhood with adult spirometric restriction were supported by meta-analysis of data from all three cohorts.

In the MAAS cohort having a low lean BMI (i.e. < 10 th percentile) at age 11 years predicted spirometric restriction at age 18: RRR 3.66 (95% CI: 1.48-9.02; $P = 0.0048$).

The association of spirometric restriction with small for gestational age, underweight in childhood, and low lean BMI in childhood was verified in those participants who had spirometric restriction and reduced total lung capacity, suggesting that these factors specifically raise the risk of lung restriction.

Notably, neither smoking nor asthma were associated with an increased risk of spirometric restriction in any of the three cohorts.

The study authors conclude: 'This study provides novel evidence that deficits in growth and nutritional

status, as early as in utero and throughout childhood, increase the risk of restricted lung volume for body size in early adult life, indicating the congenital and developmental origins of this condition.'

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Varaphani N, Stern DA, Zhai J et al. The role of growth and nutrition in the early origins of spirometric restriction in adult life: a longitudinal, multicohort, population-based study. *Lancet Resp Med* 2022;10:59-71

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