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Title: Inhaled corticosteroids and bone mineral density in children: A prospective 12-year follow-up study after early-life wheezing

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Body: Background: Inhaled corticosteroids (ICS) are the drugs of choice for asthma. Corticosteroids can have many detrimental effects on bone mineralization and growth, despite of inhaled administration. Aims and objectives: To evaluate the association between the long-term use of ICS in childhood and bone mineral density (BMD) in teenagers. Methods: Ninety-one children hospitalized for wheezing at age <24 months were prospectively followed until 12.2 (median) years of age. Data on ICS use were collected by interviewing the parents, supplemented by data from patient records. Cumulative doses, the duration of ICS use and systemic steroid doses were calculated. At the last check-up, BMD (BMDareal, g/cm2) was measured by dual energy X-ray absorptiometry (DXA) in 89 children, and apparent volumetric BMDs (aBMDvol, g/cm3) were calculated for the lumbar spine and femoral neck. Weight, height and pubertal stage were recorded. Results: The regular use of ICS at age <6 years was associated with a lower BMDareal of the lumbar spine (mean 0.76, 95%CI 0.71-0.81 vs. 0.88, 0.84-0.92; p 0.006). A lower BMDareal and aBMDvol of the femoral neck were associated with higher cumulative doses of ICS at 0–12.2 (median) years of age. Pearson's correlation coefficients were r (r2) =-0.320 (0.10) for BMDareal and r (r2) = -0.291 (0.08) for aBMDvol. Age, sex and pubertal stage were significantly associated with both BMDareal and aBMDvol, but did not confound the results. Conclusion: The use of ICS during childhood may be related to a decrease in BMD at early teenage, though the clinical manifestations of reduced BMD usually occur later in adulthood.