**DAILY INHALED STEROIDS AND BONE GROWTH**

**Scenario given:**

It is known that systemic steroids can slow bone growth. Your 8 year old asthma patient’s mother is concerned that perhaps the daily inhaled steroids (given via a metered dose inhaler or MDI) could have the same effect. What can you tell her?

**Clinical Question:**

Do daily inhaled steroids affect height?

**PICO Question:**

In pediatric patients with asthma, does administering daily inhaled steroids slow bone growth?

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| **P** | **I** | **C** | **O** |
| Pediatric with asthma | Meterdosed inhaler  MDI | Placebo | Bone growth |
| Prepubertal children | Corticosteroid | No corticosteroids | Height |
| Mild to persistent asthmatic | Inhaled corticosteroid  ICS |  | Development |
|  | Fluticasone |  | Skeletal maturation |
|  |  |  | Linear growth |

**Search Strategy:**

**Searched Terms:** “Inhaled steroids bone growth”

**Database and Articles Returned:**

Cochrane: Inhaled steroids bone growth → 10252

Cochrane: inhaled steroids bone growth/Cochrane database of systematic reviews → 1

Pubmed: Inhaled corticosteroids growth → 840

Pubmed: bone growth inhaled steroids → 76

**Filters**: humans; age birth - 19 years old; Best matches

Trip database: (asthmatic children)(inhaled corticosteroid)(height) → 232

**Selection Methods:**

Systematic reviews, meta analyses, and relevant RCTs that looked at the effect of ICS on bone growth or bone growth velocity in asthmatic children. The search yielded thousands of results that we then narrowed down based on level of evidence, sample size, date of the study, and pertinent key words used in our PICO question.

**Articles Chosen for Inclusion:**

**Influence of inhaled corticosteroid on pubertal growth and final height in asthmatic children.**

**Leonibus CD, Attanasi M, Roze Z.**

Pediatr Allergy Immunol 2016: 27: 499–506. publication 21 February 2016

DOI:10.1111/pai.12558

**Abstract**

**Background**: Controversial data exist on the possibility that inhaled corticosteroids

(ICs) affect growth in children with mild-to-moderate asthma. We assessed whether

ICs affect growth and final height (FH) in asthmatic children compared to controls.

**Methods:** A retrospective study was conducted on 113 asthmatic children compared

with 66 control children. Asthmatic children presented with mild-to-moderate asthma

and had exclusive ICs. Anthropometric data of four specific time-points were collected

for both groups (pre-puberty, onset and late puberty, and FH) and converted to

standard deviation scores (SDS). Growth trajectories were assessed as follows: (i) in

puberty, using peak height velocity (PHV) and pubertal height gain SDS (PHG-SDS);

(ii) until FH achievement, using FH-SDS and FH gain SDS (FHG-SDS). Repeated

measurement analysis was performed across longitudinal study visits. A general linear

model (GLM) was performed in asthmatic group evaluating the effect of corticosteroid

type, treatment duration, and cumulative dose on FH corrected for multiple

variables.

**Results:** At pre-puberty, height and weight SDS were similar between the groups

(p > 0.05). Height SDS progressively declined over the study period in asthmatic

patients from pre-puberty to FH (p-trend < 0.05), whereas it did not change over time

in controls (p-trend > 0.05), in both boys and girls. Asthmatic children had exclusive

ICs [budesonide (n = 36) vs. fluticasone (n = 43) vs. mometasone (n = 34)] for a mean

period of 6.25 1.20 years and a mean cumulative dose of 560.07 76.02 mg. They

showed decreased PHG-SDS and lower PHV compared to controls (all p < 0.05). FHSDS

and FHG-SDS were significantly reduced in asthmatic group compared to

controls. FH in asthmatic patients was 2.5 2.89 cm lower in boys and 2.0 2.03 cm

lower in girls than controls. The GLM showed that FH achievement was dependent on

the type of ICs, duration of the treatment, and cumulative dose (p < 0.05).

**Conclusions**: ICs affect pubertal growth determining reduced final height in asthmatic

children compared to controls, in a dose- and duration-dependent manner.

**Link:** <https://onlinelibrary.wiley.com/doi/abs/10.1111/pai.12558>

**Impact of Inhaled Corticosteroids on Growth in Children with Asthma: Systematic Review and Meta-Analysis.**

[**Loke YK**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Loke%20YK%5BAuthor%5D&cauthor=true&cauthor_uid=26191797)**1,** [**Blanco P**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Blanco%20P%5BAuthor%5D&cauthor=true&cauthor_uid=26191797)**1,** [**Thavarajah M**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Thavarajah%20M%5BAuthor%5D&cauthor=true&cauthor_uid=26191797)**1,** [**Wilson AM**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Wilson%20AM%5BAuthor%5D&cauthor=true&cauthor_uid=26191797)**1.**

[PLoS One.](https://www.ncbi.nlm.nih.gov/pubmed/26191797) 2015 Jul 20;10(7):e0133428. doi: 10.1371/journal.pone.0133428. eCollection 2015.

**BACKGROUND:** Long-term inhaled corticosteroids (ICS) may reduce growth velocity and final height of children with asthma. We aimed to evaluate the association between ICS use of >12 months and growth.

**METHODS:** We initially searched MEDLINE and EMBASE in July 2013, followed by a PubMed search updated to December 2014. We selected RCTs and controlled observational studies of ICS use in patients with asthma. We conducted random effects meta-analysis of mean differences in growth velocity (cm/year) or final height (cm) between groups. Heterogeneity was assessed using the I2 statistic.

**RESULTS:** We found 23 relevant studies (twenty RCTs and three observational studies) after screening 1882 hits. Meta-analysis of 16 RCTs showed that ICS use significantly reduced growth velocity at one year follow-up (mean difference -0.48 cm/year (95% CI -0.66 to -0.29)). There was evidence of a dose-response effect in three RCTs. Final adult height showed a mean reduction of -1.20 cm (95% CI -1.90 cm to -0.50 cm) with budesonide versus placebo in a high quality RCT. Meta-analysis of two lower quality observational studies revealed uncertainty in the association between ICS use and final adult height, pooled mean difference -0.85 cm (95% CI -3.35 to 1.65).

**CONCLUSION:** Use of ICS for >12 months in children with asthma has a limited impact on annual growth velocity. In ICS users, there is a slight reduction of about a centimeter in final adult height, which when interpreted in the context of average adult height in England (175 cm for men and 161 cm for women), represents a 0.7% reduction compared to non-ICS users.

treatment over a period of several years in children with persistent asthma.

**Link**: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4507851/>

**Inhaled Corticosteroids in Children With Persistent Asthma: Effects on Growth.**

[Cochrane Database Syst Rev.](https://www.ncbi.nlm.nih.gov/pubmed/25030198) 2014 Jul 17;(7):CD009471. Doi: 10.1002/14651858.CD009471.pub2.

[**Zhang L**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Zhang%20L%5BAuthor%5D&cauthor=true&cauthor_uid=25030198)**1,** [**Prietsch SO**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Prietsch%20SO%5BAuthor%5D&cauthor=true&cauthor_uid=25030198)**,** [**Ducharme FM**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ducharme%20FM%5BAuthor%5D&cauthor=true&cauthor_uid=25030198)**.**

**BACKGROUND**: Treatment guidelines for asthma recommend inhaled corticosteroids (ICS) as first-line therapy for children with persistent asthma. Although ICS treatment is generally considered safe in children, the potential systemic adverse effects related to regular use of these drugs have been and continue to be a matter of concern, especially the effects on linear growth.

**OBJECTIVES**: To assess the impact of ICS on the linear growth of children with persistent asthma and to explore potential effect modifiers such as characteristics of available treatments (molecule, dose, length of exposure, inhalation device) and of treated children (age, disease severity, compliance with treatment).

**SEARCH METHODS:** We searched the Cochrane Airways Group Specialised Register of trials (CAGR), which is derived from systematic searches of bibliographic databases including CENTRAL, MEDLINE, EMBASE, CINAHL, AMED and PsycINFO; we hand searched respiratory journals and meeting abstracts. We also conducted a search of ClinicalTrials.gov and manufacturers' clinical trial databases to look for potential relevant unpublished studies. The literature search was conducted in January 2014.

**SELECTION CRITERIA**: Parallel-group randomised controlled trials comparing daily use of ICS, delivered by any type of inhalation device for at least three months, versus placebo or non-steroidal drugs in children up to 18 years of age with persistent asthma.

**DATA COLLECTION AND ANALYSIS**: Two review authors independently performed study selection, data extraction and assessment of risk of bias in included studies. We conducted meta-analyses using the Cochrane statistical package RevMan 5.2 and Stata version 11.0. We used the random-effects model for meta-analyses. We used mean differences (MDs) and 95% CIs as the metrics for treatment effects. A negative value for MD indicates that ICS have suppressive effects on linear growth compared with controls. We performed a priori planned subgroup analyses to explore potential effect modifiers, such as ICS molecule, daily dose, inhalation device and age of the treated child.

**MAIN RESULTS:** We included 25 trials involving 8471 (5128 ICS-treated and 3343 control) children with mild to moderate persistent asthma. Six molecules (beclomethasone dipropionate, budesonide, ciclesonide, flunisolide, fluticasone propionate and mometasone furoate) [corrected] given at low or medium daily doses were used during a period of three months to four to six years. Most trials were blinded and over half of the trials had drop out rates of over 20%.Compared with placebo or non-steroidal drugs, ICS produced a statistically significant reduction in linear growth velocity (14 trials with 5717 participants, MD -0.48 cm/y, 95% CI -0.65 to -0.30, moderate quality evidence) and in the change from baseline in height (15 trials with 3275 participants; MD -0.61 cm/y, 95% CI -0.83 to -0.38, moderate quality evidence) during a one-year treatment period.Subgroup analysis showed a statistically significant group difference between six molecules in the mean reduction of linear growth velocity during one-year treatment (Chi² = 26.1, degrees of freedom (df) = 5, P value < 0.0001). The group difference persisted even when analysis was restricted to the trials using doses equivalent to 200 μg/d hydrofluoroalkane (HFA)-beclomethasone. Subgroup analyses did not show a statistically significant impact of daily dose (low vs medium), inhalation device or participant age on the magnitude of ICS-induced suppression of linear growth velocity during a one-year treatment period. However, head-to-head comparisons are needed to assess the effects of different drug molecules, dose, inhalation device or patient age. No statistically significant difference in linear growth velocity was found between participants treated with ICS and controls during the second year of treatment (five trials with 3174 participants; MD -0.19 cm/y, 95% CI -0.48 to 0.11, P value 0.22). Of two trials that reported linear growth velocity in the third year of treatment, one trial involving 667 participants showed similar growth velocity between the budesonide and placebo groups (5.34 cm/y vs 5.34 cm/y), and another trial involving 1974 participants showed lower growth velocity in the budesonide group compared with the placebo group (MD -0.33 cm/y, 95% CI -0.52 to -0.14, P value 0.0005). Among four trials reporting data on linear growth after treatment cessation, three did not describe statistically significant catch-up growth in the ICS group two to four months after treatment cessation. One trial showed accelerated linear growth velocity in the fluticasone group at 12 months after treatment cessation, but there remained a statistically significant difference of 0.7 cm in height between the fluticasone and placebo groups at the end of the three-year trial.One trial with follow-up into adulthood showed that participants of prepubertal age treated with budesonide 400 μg/d for a mean duration of 4.3 years had a mean reduction of 1.20 cm (95% CI -1.90 to -0.50) in adult height compared with those treated with placebo.

**AUTHORS' CONCLUSIONS:**Regular use of ICS at low or medium daily doses is associated with a mean reduction of 0.48 cm/y in linear growth velocity and a 0.61-cm change from baseline in height during a one-year treatment period in children with mild to moderate persistent asthma. The effect size of ICS on linear growth velocity appears to be associated more strongly with the ICS molecule than with the device or dose (low to medium dose range). ICS-induced growth suppression seems to be maximal during the first year of therapy and less pronounced in subsequent years of treatment. However, additional studies are needed to better characterise the molecule dependency of growth suppression, particularly with newer molecules (mometasone, ciclesonide), to specify the respective role of molecule, daily dose, inhalation device and patient age on the effect size of ICS, and to define the growth suppression effect of ICS.

**Link:** <http://cochranelibrary-wiley.com/doi/10.1002/14651858.CD009471.pub2/abstract;jsessionid=7F41CF0F17D601E965DE12E9747D5787.f02t04>

**Effect of Inhaled Glucocorticoids in Childhood on Adult Height.**

[**Kelly HW**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Kelly%20HW%5BAuthor%5D&cauthor=true&cauthor_uid=22938716)**1,** [**Sternberg AL**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Sternberg%20AL%5BAuthor%5D&cauthor=true&cauthor_uid=22938716)**,** [**Lescher R**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Lescher%20R%5BAuthor%5D&cauthor=true&cauthor_uid=22938716)**,** [**Fuhlbrigge AL**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Fuhlbrigge%20AL%5BAuthor%5D&cauthor=true&cauthor_uid=22938716)**,** [**Williams P**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Williams%20P%5BAuthor%5D&cauthor=true&cauthor_uid=22938716)**,** [**Zeiger RS**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Zeiger%20RS%5BAuthor%5D&cauthor=true&cauthor_uid=22938716)**,** [**Raissy HH**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Raissy%20HH%5BAuthor%5D&cauthor=true&cauthor_uid=22938716)**,** [**Van Natta ML**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Van%20Natta%20ML%5BAuthor%5D&cauthor=true&cauthor_uid=22938716)**,** [**Tonascia J**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Tonascia%20J%5BAuthor%5D&cauthor=true&cauthor_uid=22938716)**,** [**Strunk RC**](https://www.ncbi.nlm.nih.gov/pubmed/?term=Strunk%20RC%5BAuthor%5D&cauthor=true&cauthor_uid=22938716)**;** [**CAMP Research Group**](https://www.ncbi.nlm.nih.gov/pubmed/?term=CAMP%20Research%20Group%5BCorporate%20Author%5D)**.**

N Engl J Med. 2012 Sep 6;367(10):904-12. doi: 10.1056/NEJMoa1203229

**BACKGROUND**: The use of inhaled glucocorticoids for persistent asthma causes a temporary reduction in growth velocity in prepubertal children. The resulting decrease in attained height 1 to 4 years after the initiation of inhaled glucocorticoids is thought not to decrease attained adult height.

**METHODS**: We measured adult height in 943 of 1041 participants (90.6%) in the Childhood Asthma Management Program; adult height was determined at a mean (±SD) age of 24.9±2.7 years. Starting at the age of 5 to 13 years, the participants had been randomly assigned to receive 400 μg of budesonide, 16 mg of nedocromil, or placebo daily for 4 to 6 years. We calculated differences in adult height for each active treatment group, as compared with placebo, using multiple linear regression with adjustment for demographic characteristics, asthma features, and height at trial entry.

**RESULTS:** Mean adult height was 1.2 cm lower (95% confidence interval [CI], -1.9 to -0.5) in the budesonide group than in the placebo group (P=0.001) and was 0.2 cm lower (95% CI, -0.9 to 0.5) in the nedocromil group than in the placebo group (P=0.61). A larger daily dose of inhaled glucocorticoid in the first 2 years was associated with a lower adult height (-0.1 cm for each microgram per kilogram of body weight) (P=0.007). The reduction in adult height in the budesonide group as compared with the placebo group was similar to that seen after 2 years of treatment (-1.3 cm; 95% CI, -1.7 to -0.9). During the first 2 years, decreased growth velocity in the budesonide group occurred primarily in prepubertal participants.

**CONCLUSIONS**: The initial decrease in attained height associated with the use of inhaled glucocorticoids in prepubertal children persisted as a reduction in adult height, although the decrease was not progressive or cumulative.

**Link**: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3517799/>

**Effects of Beclomethasone and Factors Related to Asthma of the Growth of Prepubertal Children.**

**Camargos PA, Lasmar LM.**

Respir Med. 2010 Jul;104(7):951-6. doi: 10.1016/j.rmed.2010.02.002

**Abstract**

Few studies on the concomitant effects of beclomethasone dipropionate and asthma-related factors on the growth of prepubertal asthmatic children have been published to date. In this prospective long-term 'real-life' cohort study we recruited 82 prepubertal steroid-naïve asthmatic patients aged 3 + years, excluding those with birth weight lower than 2500 g, malnutrition, and other concurrent chronic diseases. Height/age and weight/age Z scores were calculated every three months. Random effects multivariate longitudinal data analysis was used to adjust height/age and weight/age Z scores with independent variables. Among the studied patients, 63.4% were male, aged 4.7 + or - 1.5 years, 68.3% suffered from severe persistent asthma and had normal values for height/age and weight/age Z scores at enrolment. They were followed for 5.2 years (range 2.3-6.1) and used a mean daily beclomethasone dipropionate dose of 351.8 mcg (range 137.3-1140.0). Height/age and weight/age Z scores were not affected by either duration of treatment or doses of beclomethasone dipropionate up to 500 mcg, 750 mcg and higher than 750 mcg (p-values > 0.17). The multivariate analysis final model showed that severe persistent asthma was associated to lower height for age Z score (p = 0.04), whereas hospitalizations because of acute asthma (before and during follow-up) were associated (p = 0.02) to lower weight for age Z score. Growth parameters were not affected by the use of beclomethasone dipropionate.

**Link**: https://www.ncbi.nlm.nih.gov/pubmed/

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| Author (Date) | Level of Evidence | Sample/Setting  (# of subjects/ studies, cohort definition etc. ) | Outcome(s) studied | Key Findings | Limitations and Biases |
| [Zhang L](https://www.ncbi.nlm.nih.gov/pubmed/?term=Zhang%20L%5BAuthor%5D&cauthor=true&cauthor_uid=25030198).1., [Prietsch S.O](https://www.ncbi.nlm.nih.gov/pubmed/?term=Prietsch%20SO%5BAuthor%5D&cauthor=true&cauthor_uid=25030198)., [Ducharme F.M](https://www.ncbi.nlm.nih.gov/pubmed/?term=Ducharme%20FM%5BAuthor%5D&cauthor=true&cauthor_uid=25030198).  (2014) | | Systematic Review | 25 RCTs, 8741 participants, children under 19 years old, with mild-to-moderate asthma | Primary outcome:  -Linear growth velocity  Secondary outcomes:  -Change in height standard deviation over time  -change from baseline height in cm over time  -change in height z-score over time | -ICS is associated with a decrease of 0.47 cm/y (95% CI -0.66 to -0.27, P value <0.00001) and 0.48 cm/y (95% CI -0.65 to -0.30, P value <0.00001) in linear growth velocity in the first year of usage.  -A decrease from baseline height was seen in the first year, as well as a -0.13 (95% CI -0.24 to -0.01, P value 0.03) change in height standard deviation.  -No statistically significant decrease in linear growth velocity or change in baseline height in the second year of ICS treatment.  -A reduction of 1.2 cm (95% CI -1.90 to -0.50, P value 0.001 ) was noted at adult height  Summary:  ICS has the largest effect on height in the first year, there is minimal effect after that. | -Trials were screened for this review by title and/or abstract, rather than the entire article. This may have left room for relevant articles to be excluded from the review  -11 of the RCTs did not give a detailed explanation of their method for randomization, 6 of the RCTs included did not provide their method of randomization at all, this leaves room for a potential bias in the original trials that were included in the review |

Summary of Evidence

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| Kelly HW, Sternberg AL, Lescher R, Fuhlbrigge AL, Williams P, Zeiger RS, Raissy HH, Van Natta ML, Tonascia J, Strunk RC; CAMP Research Group. (2012) | Randomized control trial | 1041 children between ages 5 and 13 years with mild-to-moderate asthma were randomly assigned into three groups: budesonide group, nedocromil group, and placebo group | -Adult height  -Growth velocity  -Effects of glucocorticoid dose | -The average adult height was 1.2 cm lower in the budesonide group than in the placebo group (171.1cm vs. 172.3cm, P=0.001, CI=95%), and the average adult height in the nedocromil group was 0.2 cm lower than the placebo group (172.1cm vs 172.3cm, P=0.61, CI=95%)  -The difference in velocity reduction that was seen in the first 2 years of assigned treatment in the budesonide group compared with the placebo group (boys with P<0.001, and girls with P=0.007)  -A larger daily dose was associated with a lower adult height (-0.1 cm for each microgram per kilogram of body weight, P=0.007)  -The adult height in budesonide group were similar to placebo group after 2 years of treatment (-1.3cm, 95% CI) | -805 out of 1041 subjects are White, and 621 out of 1041 are male  - Information of subjects’ health and medication use was obtained by telephone contacts→ hard to reach respondents; can not elicit better response like in face to face interview; reliability of reporting is questionable  -In this study, 98 subjects were lost to follow up, and imputation method was used to fill in missing data, which may affect statistical analyses |

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| Leonibus CD, Attanasi M, Roze Z, (2016) | Retrospective Case-control | 113 asthmatic children with mild-moderate asthma and 33 control children retrospectively chosen from Endocrine Clinic for endocrine diseases not affecting growth and pubertal development | Primary outcome:  - assess longitudinally from prepubertal age to attainment of final height  - the effect of inhaled corticosteroid therapy on growth  - final height in children with mild-moderate asthma compared to control population  Secondary outcome:  - type, duration, and dose of IC therapy had effect on final height | - The final height in asthmatic boys was 2.5 cm ± 2.89 [mean (SD) 173.55 (3.79) vs. 176.04 (2.37), p= 0.028] cm compared to controlled boys  - final height of asthmatic girls was 2.0 ± 2.03 [mean (SD) 161.16 (4.79) vs. 163.44 (3.49), p=0.047] cm compared to the controlled girls  - statistically significant decrease in pubertal height gain SDS in asthmatic group for boys [-0.21 (0.89) vs 0.03 (0.41), p=0.036]  - statistically significant decrease in pubertal height gain SDS in asthmatic group for girls [ -0.36 (0.93) vs 0.02 (0.48) SDS, p=0.012]  - mean height SDS declined in asthmatic group from pre-puberty to FH from 0.26 (0.82) to -0.29 (0.65) in boys, girls 0.40 (0.96) to -0.17 (0.79) p<0.05 while the control group did not significantly change from 0.16 (0.64) to 0.20 (0.59) SDS in boys, while girls from 0.15 (0.65) to 0.19 (0.55) SDS, p>0.05 | - The study had several participants in which the final height measurement was not taken due to drop out and the authors did not include their data in study  - The authors do not inform the readers of the age range and other demographics of the experimental and control group  - the authors understand and state that there might be some selection bias  - the authors did not specifically looked at the bone age and biochemical markers of puberty  - A limitation that is not mentioned is that the study was done in italy and the population might be more homogenous in population and should be taken into consideration when looking at the results |

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| Loke, YK., Blanco, P., Thavarajah, M., Wilson, A.M. (2015) | Systematic Review and Meta-Analysis | 23 RCTs, 3 observational studies on children with asthma of any severity | Growth Velocity  Final Adult Height | Growth velocity: Pooled mean difference -0.48 cm/year (95% CI -0.66-0.29 cm/yr)  Final adult height: Pooled mean difference of -1.2 cm (95% CI -1.9 - 0.5 cm)  Observational studies found 0.7-0.9 cm reduction in final adult height (95% CI -3.35-1.65, I2=0%) | Section called “risk bias assessment” describes criteria used by two reviewers to filter and score selected studies. A third final reviewer than evaluated the previous reviewers’ results. Their specific qualifications are listed.  The study did not list a demographics table.  They included two extra observational studies in a review that comprises RCTs. Although they used it primarily to better understand the results from their meta-analysis, it could have imposed some bias. |
| Camargos PA, Lasmar LM. (2010) | Prospective long-term cohort study | Cohort following 82 prepubertal asthmatic patients at 3 month intervals till age 9/9.5y/o. -Severe persistent | - Height/age Z-scores  - Weight/age Z scores -  - Growth Velocity | Of non-users and BDP users (500mcg/day): no deviation between height and weight when compared to national growth chart.  (p-values >0.17) - not significant  Similar results found with higher dosed BDP (500-750mcg/day) with no deviation after age 5 when compared to national growth chart.  (p-values >0.17) - not significant  Multivariate analysis final model showed that “severe persistent asthma” was associated to lower height for age Z score (p = 0.02), scores 0.47 SD lower than pts with “moderate asthma” - not significant since  Values fall within range of Z score | Participants (majority male) came from low-income families and with mother of low education status. Although this study states they were well nourished and of average height/weight, the SES of the pts should be noted.  Another limitation is the use of the USNC for Health Statistics/CDC growth chart for participants living in Brazil |

**Conclusion(s):**

Both meta analyses concluded (reviewing 23-25 RCTs each) that the use of Inhaled Corticosteroids for asthma in pediatric populations results in less than a 1.2 cm decrease in final adult height. The systematic reviews also found <0.66 decrease in bone growth velocity (Zhang et. Al., 2014, Loke et. al., 2015).

Certain studies found greater changes in height than others. As stated previously, the two meta-analyses (Zhang et. al., 2014, Loke et. al., 2015) found a decrease in adult height of 1.2cm whereas the case-control (Leonibus et al., 2016) found a decrease in height by 2.5 cm for boys and 2.2 cm in girls. Moreover, the prospective long-term cohort also found a decrease in childhood height; however, it was not statistically significant (Camargos & Lasmar, 2010).

When deciding which of these findings should be more heavily weighted, the level of evidence should be considered; the Leonibus et. al. is a case-control that used a homogenous population of mainly Eastern European Caucasians because the study was conducted in Italy (2016). The two meta-analyses, on the other hand, uses larger sample sizes from many studies giving it more power.

**Clinical Bottom Line:**

Changes in adult height and growth velocity are minimal when considering the risks associated with the disuse of ICS for pediatric asthmatic patients. As such, pediatric asthmatic patients should continue to use ICS to prevent asthma exacerbations and further complications.

When discussing the side effects of ICS to the family of the patients, we would inform them there would likely only be a decrease in height of about 1.2cm, but it could result in a decrease in height of 2.5 cm for boys and 2.2 cm in girls.

In conclusion, our clinical recommendation was based on the evidence primarily found in the two major meta analyses and systematic reviews analyzed.