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# Asthma, Bones & Corticosteroids: Are inhaled corticosteroids associated with fractures in children with asthma?

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**Abstract:**

**Aim**: The prevalence of asthma worldwide among older children varies between 10 and 20%. One of the most effective therapies to treat asthma and prevent exacerbations is inhaled corticosteroids (ICS). Systemic corticosteroids are known to decrease bone mineral density (BMD) and increase the risk of fractures among children, but little is known about the effect of ICSs on fracture risk in children with asthma. The aim of this study was to investigate the fracture rates in children with asthma using ICSs. **Methods**: A survey on fracture history and risk, bone health and asthma was administered by a researcher to children aged 6-18 years attending a tertiary care children's hospital in Melbourne, Australia over a six month period. Fracture risks were compared in children on low or high dose ICS with those not on any ICS and non-asthmatics. **Results**: 216 healthy control participants were compared with 211 children with asthma - 22% (n=46) on low dose ICS therapy, 44% (n=94) on high dose ICS, and 34% (n=71) not on any ICS. There was no difference in the incidence of fractures between children with asthma (24.6% n=53) and healthy controls (24% n=51) (Ç^2=0.132; p=0.717). There were no differences in fracture incidence in the subgroups of children with asthma (p=0.695). **Conclusion:** ICS use was not associated with fracture risk in children with asthma.

***Keywords:*** *Endocrinology, Respiratory, Pharmacology*

***What is already known on this topic?***

- Inhaled corticosteroids are the mainstay of asthma therapy in children with asthma
- It is known that low dose ICS use does not have significant effects on bone mineral density
- Effect of high doses of inhaled corticosteroids (ICS) on fracture risk in children with asthma has not been studied adequately

***What this paper adds?***

- No significant differences in fracture risk among high and low dose ICS users
- No increased risk of fractures among children with asthma compared to non-asthmatic controls
- Predefined risk factors did also not seem to have an effect on the risk of fractures in children with asthma compared with healthy controls. Large cohort studies with long follow-ups in

which the time relation between ICS and fracture occurrence is known are necessary to determine the longer-term effects of ICS on bone health and safety in children with asthma.

**Main text:**

**Introduction:**

The prevalence of asthma worldwide among children, between 6 and 18 years, varies between 10 and 20%.[1] One of the most effective therapies to treat asthma and prevent exacerbations is inhaled corticosteroids (ICS).[2-4] Systemic corticosteroids are known to decrease bone mineral density (BMD) and therefore are associated with a higher risk of fractures among children.[5-6] Although ICSs are generally considered safe, their effects on fracture risk in children with asthma still remains unclear.[7-8] Fractures occur commonly in children; Cooper *et al*.[9] has reported a fracture risk of 33% among children 0 to 17 years of age.

Recent studies indicate that high dose ICSs and oral corticosteroids are associated with decreased BMD, and a dose-dependent increased risk of fractures in adults.[10-11] The effect of high doses of ICS on fracture risk in children with asthma still remains unclear.[12-19] There is currently no established protocol or guidelines on how to monitor bone health in children with asthma and limited BMD data in the paediatric asthma population. Uncertainty regarding safety of ICS and fracture risk can potentially translate to poor prescriber adherence to treatment guidelines, poor patient adherence to ICS therapy and poor asthma control. The primary aim of this study was to investigate the association between fracture risk and ICS use (high and low doses) in children. Secondary aims were to explore the effects of age, pubertal status, calcium intake and body mass index (BMI) on fracture risk.

**Materials and Methods:**

*Study design and setting:*

A questionnaire study was performed to be able to perform a retrospective follow up study to evaluate the association between ICS use and fracture risk. The study was conducted between September 2015 and January 2016 at The Royal Children's Hospital (RCH) in Melbourne, Australia. The RCH is the largest paediatric hospital in Victoria and one of the biggest in Australia, with more than 240,000 specialist clinic appointments and 36,000 overnight stays annually.

*Participant identification and recruitment:*

Eligible patients with asthma were recruited from the respiratory and allergy clinics, and the emergency department of the RCH. Potential participants were also flagged to the researchers during

department meetings, lung function testing and referred by respiratory and general medicine clinicians. Control participants (with no diagnosis of asthma) were recruited through the dental clinics of RCH while waiting for their appointment. A questionnaire and consent form were handed to eligible participants or their parents/guardians. All study participants signed the informed consent form prior to completing the questionnaire. Children under the age of 14 years were required to have parental/guardian consent.

*Inclusion criteria*

Children with asthma aged between 6 and 18 years with a clinical diagnosis of asthma were included. Within this group, three sub-groups were formed: 1) children with asthma and using doses of ICSs (e250µg BDP-HFA per day) for e 6 months; 2) children with asthma and using low doses of ICSs (<250µg BDP-HFA per day) for e 6 months; and 3) children with asthma who were not taking any ICSs These cut-off doses are in line with the National Asthma Guidelines for Paediatric Asthma[3], and BDP-HFA equivalent dosing, as it is widely used, was chosen for ease of conversion.

Children aged between 6 and 18 years, who neither had a clinical diagnosis of asthma nor a history of ICS use were also included and formed the non-asthmatic control group.

*Exclusion criteria*

Children were excluded if they had a history of previous or current use of bisphosphonates or other medication with a known clinical effect on the skeletal bone mineral density (e.g. anti-epileptic medication), or if they had a known primary bone disorder documented in the medical records (e.g. osteogenesis imperfecta). Furthermore, patients were excluded if they could not speak or write English, to prevent misinterpretation of the questionnaire.

*Data collection:*

The questionnaire consisted of three parts: a bone health and injury questionnaire, an asthma and corticosteroids questionnaire and the Asthma Control Questionnaire (ACQ).[20] The bone health and injury questionnaire was used in a previous bone health project investigating fracture risk in children with epilepsy.[21] The asthma and corticosteroids questionnaire was developed by the investigatory team and was piloted in children 6 years and over (n=10). The questions on the use of ICS were directed at current exposure (the use of ICS during the period the questionnaire was filled up). The

questionnaires were completed by the parent/guardian on behalf of children under 12 years of age except for the ACQ which was completed by the child as recommended.[20] Children older than 12 years were eligible to complete the written questionnaire themselves but under parental supervision to reduce recall bias/missing data. Children with asthma underwent spirometry voluntarily to provide forced expiratory volume in one second ($FEV_1$), which allowed completion of the 7-item ACQ. Where spirometry could not be performed on the day, the recent lung function test result (within four weeks) was sourced from Medical records. Only the ACQ-6 score (i.e. without lung function data) was used if where there was no $FEV_1$ score. All children with asthma were compared using the ACQ-6 score, then ACQ-7 comparisons were made only when the data were available.

*Primary outcome:*

The primary outcome was the incidence of self-reported fractures in their lifetime (grouped into forearm/wrist, upper leg, lower leg, hip, ankle, toe/foot, upper arm, other or multiple). Information regarding age at the time of the incident, cause of fracture and treatment was also captured.

The incidence of fractures in the two groups were compared after adjusting for age, body mass index (BMI), pubertal status (based on age groups 6-9, 10-14 and 15-18 years old), exposure to household smoking, history of bone health medication, calcium intake, family history of osteoporosis and weekly physical activity levels.

*Ethics approval*

This project was approved by The Royal Children's Hospital Human Research Ethics Committee; HREC #35167 and The Monash University Human Research Ethics Committee CF15/3391-2015001446.

*Statistical analysis:*

All data were analysed using the Statistical Package for Social Sciences (SPSS), version 22.0 (IBM, Somers, NY, USA, 2010). A Pearson Chi-square was used to test the difference in the incidence of fractures between children with asthma and healthy controls. A Mann Whitney U test was used to estimate group differences in fracture risks within the different groups of children with asthma. Binary logistic regression was used to investigate the effects of confounding factors on the incidence of fractures in asthmatic children. The significance level was fixed at $p<0.05$. This form of analysis builds a binary prediction model (analogous to a linear regression model) where the significance of the regression coefficient can be associated with a significant influence on the model's accuracy.

**Results:**

Out of 582 eligible patients with asthma identified through medical records, 453 were approached during their clinic appointments (Figure 1). A total of 220 patients with asthma completed the questionnaire (participation rate of 49%). Out of the 311 randomly selected controls who were approached by convenience sampling, 255 participated (participation rate of 82%). After six months of recruitment, the final numbers of participants (Table 1) after applying the exclusion/inclusion criteria were: 211 children with asthma (62% males and mean [SD] age 11.12[3.3]) and 216 controls (46% males and mean [SD] age 11.1[3.4]). No significant difference in age, BMI classification and ethnicity were found between groups; however, there were significantly more males among the children with asthma 61,6% vs 46.3% (p=0.002).

Figure 1. Overview of participant recruitment strategy

Among the 211 children with asthma, 46 (22%) were using a low dose ICS, 94 (44%) a high dose ICS and 71 (34%) had no history of ICS use at the time of the interview. There was a significant difference between the groups regarding control of symptoms since diagnosis (Table 2); children with low dose ICS had the highest percentage of improvement of symptoms (p=0.029). There was also a significant difference in the number of self- reported asthma attacks since diagnosis (p=0.007), and history of hospitalization/emergency room visits (p=0.005) where ICS users had the higher percentages compared with no ICS users. An asthma action plan was possessed by 91% of the high dose ICS users compared with 89% of low dose ICS users and 70% of no ICS users (p=0.001). Self-reported adherence between the high and low ICS groups showed a significant difference (p=0.032), low dose ICS users claimed that they always remember to take their asthma medication (59%); however, among non-users and high dose ICS users the percentages were all above 50%. Although physical activity levels between ICS users and asthmatic non-ICS users differed significantly (p=0.028) they did not significantly differ between the different ICS groups (p=0.102).

A total of 104 individuals of the 427 participants (children with asthma and healthy controls) sustained one or more self-reported fractures, giving a fracture incidence of 24.4% in the population (Table 3). The incidence of fractures within the different groups were 24% in controls, 21% in asthmatic non-ICS users, 24% in low dose ICS users and 29% in high dose ICS users. When comparing the fracture incidences between the control group and the different subgroups of children with asthma, there were no significant differences (p=0.695). Most fractures (44%) occurred at mid

pubertal age (10-14 years old) with a median of 11.1 years among both groups. There was no difference in the incidence of fractures between the index group (24,6% n=53) and controls (24% n=51) (Ç^2=0.132 p=0.717) nor within the index group (p=0.695). In a binary logistic regression model adjusting for potential confounders including age, pubertal status, BMI, exposure to household smoking, history of bone health supplement use, dietary calcium intake, family history of osteoporosis and activity levels, there was no significant difference in the incidence of fractures between the ICS groups (p = 0.398).

***Table 1: Demographics of the study participants at baseline***

| | | Children with asthma (n=211) | | Controls (n=216) | | Difference between groups |
|---|---|---|---|---|---|---|
| | | n/mean | (%/SD) | n/mean | (%/SD) | |
| Male | | 130 | (62%) | 100 | (46%) | .002 |
| Age in years, mean (SD) | | 11.1 | (3.3) | 11.1 | (3.4) | |
| Pubertal status | Pre pubertal (6-9yo*) | 78 | (37%) | 80 | (37%) | .46 |
| | Mid pubertal (10-14yo) | 91 | (43%) | 88 | (41%) | |
| | Peri pubertal (15-18yo) | 42 | (20%) | 48 | (22%) | |
| BMI | <5th % (classified as underweight)** | 11 | (5%) | 17 | (8%) | .50 |
| | 5th-85th % (classified as normal weight)** | 139 | (66%) | 133 | (62%) | |
| | 85th-95th % (classified as overweight)** | 39 | (18%) | 37 | (17%) | |
| | >95% (classified as obese)** | 22 | (10%) | 29 | (13%) | |
| Ethnicity | Caucasian | 162 | (77%) | 167 | (77%) | .20 |
| | Asian | 26 | (12%) | 22 | (10%) | |
| | Other | 23 | (3%) | 27 | (6%) | |
| Smoking | Current Smoker | 1 | (0%) | 2 | (1%) | .58 |
| | Smoker at home | 49 | (23%) | 45 | (21%) | .55 |
| Pets | Yes | 128 | (61%) | 143 | (66%) | .24 |
| Other medical conditions | Allergy | 120 | (57%) | 4 | (2%) | .00 |
| | Cardiovascular | 7 | (3%) | 9 | (4%) | .66 |
| | Dermatological | 22 | (10%) | 1 | (0%) | .00 |
| | Endocrine | 10 | (5%) | 9 | (4%) | .76 |
| | Gastro intestinal | 8 | (4%) | 13 | (6%) | .19 |
| | Neurological | 7 | (3%) | 10 | (5%) | .50 |
| | Psychological | 9 | (4%) | 12 | (6%) | .55 |
| | Respiratory | 211 | (100%) | 1 | (0%) | .00 |
| | Genetic | 1 | (0%) | 8 | (4%) | .021 |
| Activity levels | 0hrs/week | 5 | (2%) | 21 | (10%) | .028 |

| | | | | | |
|---|---|---|---|---|---|
| 1-3hrs/week | 54 | (26%) | 59 | (27%) | |
| 4-6hrs/week | 60 | (28%) | 54 | (25%) | |
| 5-9hrs/week | 43 | (20%) | 38 | (18%) | |
| >10hrs/week | 49 | (23%) | 44 | (20%) | |

**yo = years old*

*** According to The National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion. [Internet] Body mass index-for-age percentiles. 2000, cited; Available from: http://www.cdc.gov/growthcharts*

***Table 2: Demographics of the study participants with asthma at baseline***

| Demographic | | No ICS | | Low dose ICS | | High dose ICS | | Difference between groups |
|---|---|---|---|---|---|---|---|---|
| | | n/mean | (%/SD) | n/mean | (%/SD) | n/mean | (%/SD) | |
| N | | 71 | | 46 | | 94 | | |
| Age in years | | 11.0 | (3.1) | 9.35 | (3.0) | 12,06 | (3,3) | |
| Age in years at diagnosis | | 5.75 | (3.8) | 3.63 | (3.2) | 3.57 | (2.8) | |
| Male | | 45 | (63%) | 23 | (50%) | 62 | (66%) | .18 |
| Medication | | 71 | (100%) | 46 | (100%) | 94 | (100%) | |
| | salbutamol | 67 | (94%) | 43 | (93%) | 92 | (98%) | .38 |
| | fluticasone + salmeterol | 0 | (0%) | 8 | (17%) | 40 | (43%) | .000 |
| | fluticasone | 0 | (0%) | 25 | (54%) | 28 | (30%) | .000 |
| | ciclesonide | 0 | (0%) | 9 | (20%) | 5 | (5%) | .000 |
| | budesonide + eformoterol | 0 | (0%) | 2 | (4%) | 19 | (20%) | .000 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | budesonide | 0 | (0%) | 0 | (0%) | 1 | (1%) | .54 |
| | Other ICS | 0 | (0%) | 2 | (4%) | 0 | (0%) | .027 |
| Activity levels | 0h/week | 0 | (0%) | 0 | (0%) | 5 | (5%) | .10 |
| | 1-3h/week | 17 | (24%) | 14 | (30%) | 23 | (24%) | |
| | 2-6h/week | 20 | (28%) | 9 | (20%) | 31 | (33%) | |
| | 7-9h/week | 12 | (17%) | 12 | (26%) | 19 | (20%) | |
| | >10h/week | 22 | (31%) | 11 | (24%) | 16 | (17%) | |
| Asthma symptoms since diagnosis | Improved | 29 | (41%) | 33 | (72%) | 9 | (10%) | .029 |
| | Stayed the same | 23 | (32%) | 16 | (35%) | 7 | (7%) | |
| | Worsened | 33 | (46%) | 32 | (70%) | 19 | (20%) | |
| Asthma exacerbations since diagnosis | None | 27 | (38%) | 11 | (24%) | 14 | (15%) | .007 |
| | 1-10 attacks | 30 | (42%) | 19 | (41%) | 32 | (34%) | |
| | 11-20 attacks | 3 | (4%) | 11 | (24%) | 10 | (11%) | |
| | 21-30 attacks | 5 | (7%) | 1 | (2%) | 8 | (9%) | |
| | >30 attacks | 6 | (8%) | 4 | (9%) | 20 | (21%) | |
| Hospitalization/ emergency department visits | | 30 | (42%) | 31 | (67%) | 61 | (65%) | .005 |
| Asthma triggers | Aeroallergens | 54 | (76%) | 35 | (76%) | 77 | (82%) | .59 |
| | Exercise | 20 | (28 | 8 | (17 | 30 | (32 | .19 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | %) | | %) | | %) | |
| | Viral infection | 30 | (42 %) | 25 | (54 %) | 49 | (52 %) | .34 |
| | Medication | 1 | (1% ) | 0 | (0% ) | 5 | (5% ) | .14 |
| Family history of Asthma | Maternal | 20 | (28 %) | 14 | (30 %) | 22 | (23 %) | .20 |
| | Paternal | 9 | (13 %) | 2 | (4% | 11 | 12% | |
| | Siblings | 4 | (6% ) | 5 | (11 % | 7 | (7% | |
| | Other | 17 | (24 %) | 10 | (22 % | 34 | (36 % | |
| Frequency of lung function monitoring | Monthly | 3 | (4% ) | 5 | (11 % | 8 | (9% ) | .000 |
| | Quarterly | 9 | (13 %) | 13 | (28 %) | 28 | (30 %) | |
| | 6-monthly | 8 | (11 %) | 11 | (24 %) | 31 | (33 %) | |
| | Yearly | 24 | (34 %) | 10 | (22 %) | 13 | (14 %) | |
| Asthma action plan YES | | 50 | (70 %) | 41 | (89 %) | 86 | (91 %) | .001 |
| Adherence to asthma medication (2) | Always | 41 | (58 %) | 27 | (59 %) | 52 | (55 %) | .032 |
| | Most of the time | 16 | (23 %) | 18 | (39 %) | 35 | (37 %) | |
| | Sometimes | 7 | (10 %) | 1 | (2% ) | 6 | (6% ) | |
| | Rarely | 4 | (6% ) | 0 | (0% ) | 1 | (1% ) | |
| | Hardly any of the time | 3 | (4% ) | 0 | (0% ) | 0 | (0% ) | |
| Oral corticosteroid use (burst therapy) in the past 6 months | 0 | 57 | (80 %) | 31 | (67 %) | 54 | (57 %) | .06 |
| | 1 | 10 | (14 | 9 | (20 | 21 | (22 | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | %) | | %) | | %) | |
| | 2 | 1 | (1% | 3 | (7% | 12 | (13 | |
| | | | ) | | ) | | %) | |
| | >3 | 3 | (4% | 3 | (7% | 7 | (7% | |
| | | | ) | | ) | | ) | |
| ACQ-6 + | Good control | 47 | (66 | 33 | (72 | 56 | (60 | .12 |
| | | | %) | | %) | | %) | |
| | Poor control | 18 | (25 | 10 | (22 | 36 | (38 | |
| | | | %) | | %) | | %) | |
| ACQ-7 + | Good control | 35 | (49 | 26 | (57 | 46 | (49 | .06 |
| | | | %) | | %) | | %) | |
| | Poor control | 9 | (13 | 9 | (20 | 31 | (33 | |
| | | | %) | | %) | | %) | |

*+ ACQ is Asthma Control Questionnaire*[20]

***Table 3: Characteristics of fractures in children with asthma and healthy controls at baseline***

| | | Control | | Asthmatic no ICS | | Low dose ICS | | High dose ICS | | Difference between groups |
|---|---|---|---|---|---|---|---|---|---|---|
| | | n/mean | % | n/mean | % | n/mean | % | n/mean | % | |
| N | | 216 | | 71 | | 46 | | 94 | | |
| Fractures | Yes | 51 | (24%) | 15 | (21%) | 11 | (24%) | 27 | (29%) | .70 |
| Number of fractures | 1 | 42 | (19%) | 12 | (17%) | 8 | (17%) | 18 | (19%) | .62 |
| | 2 | 8 | (4%) | 1 | (1%) | 2 | (4%) | 4 | (4%) | |
| | >3 | 2 | (1%) | 2 | (3%) | 1 | (2%) | 5 | (5%) | |
| Fracture site | Forearm/wrist | 7 | (3%) | 7 | (10%) | 3 | (7%) | 6 | (6%) | .43 |
| | Fingers | 5 | (2%) | 2 | (3%) | 2 | (4%) | 5 | (5%) | |
| | Upper leg | 2 | (1%) | 1 | (1%) | 1 | (2%) | 1 | (1%) | |
| | Lower leg | 1 | (0%) | 0 | (0%) | 2 | (4%) | 1 | (1%) | |
| | Hip | 0 | (0%) | 0 | (0%) | 0 | (0%) | 1 | (1%) | |
| | Ankle | 2 | (1%) | 0 | (0%) | 0 | (0%) | 0 | (0%) | |
| | Toe/foot | 0 | (0%) | 2 | (3%) | 0 | (0%) | 1 | (1%) | |
| | Upper arm | 6 | (3%) | 1 | (1%) | 1 | (2%) | 3 | (3%) | |
| | Other | 1 | (0%) | 0 | (0%) | 0 | (0%) | 1 | (1%) | |
| | Multiple | 8 | (4%) | 2 | (3%) | 2 | (4%) | 8 | (9%) | |
| Household smoking | | 45 | (21%) | 17 | (24%) | 13 | (28%) | 19 | (20%) | .67 |
| Bone health supplement use | Calcium | 1 | (0%) | 2 | (3%) | 1 | (2%) | 1 | (1%) | .82 |
| | Vitamin D | 13 | (6%) | 4 | (6%) | 3 | (7%) | 8 | (9%) | |
| | Calcium & Vitamin D | 6 | (3%) | 2 | (3%) | 2 | (4%) | 5 | (5%) | |
| Dietary calcium intake | > Daily recommendation | 64 | (30%) | 18 | (25%) | 11 | (24%) | 23 | (24%) | .71 |
| | < Daily recommendation | 152 | (70%) | 53 | (75%) | 35 | (76%) | 71 | (76%) | |
| Family history of osteoporosis | | 35 | (16%) | 21 | (30%) | 11 | (24%) | 25 | (27%) | .34 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Physical activity level | 0h/week | 21 | (10%) | 0 | (0%) | 0 | (0%) | 5 | (5%) | .05 |
| | 1-3hr/week | 59 | (27%) | 17 | (24%) | 14 | (30%) | 23 | (24%) | |
| | 2-6hr/week | 54 | (25%) | 20 | (28%) | 9 | (20%) | 31 | (33%) | |
| | 5-9hr/week | 38 | (18%) | 12 | (17%) | 12 | (26%) | 11 | (12%) | |
| | >10hr/week | 44 | (20%) | 21 | (30%) | 11 | (24%) | 16 | (17%) | |

**Discussion:**

Overall, there were no significant differences in the incidences of fractures among different groups after adjusting for age, pubertal status, BMI scale, exposure to household smoking, history of bone health supplement use, dietary calcium intake, family history of osteoporosis and physical activity levels. Even though there were significant differences between children with asthma and healthy controls in gender and activity levels, these were not found to be significant in affecting a fracture risk. A number of studies have examined the influence of ICS on BMD in asthmatic children but there was a great disparity in their outcomes.[7,11] Kelly *et al*.[8] reported ICS to be associated with BMD and final adult height but did mention that ICS use can reduce the need for oral corticosteroid therapy which has a greater influence on BMD. Schlienger *et al*.[13] conducted a population-based nested case-control study and Van Staa *et al*.[14], conducted a population-based cohort study to investigate fracture risk in children using ICS in the United Kingdom. Schlienger *et al*.[13] concluded that ICS use was not associated with a higher risk of fracture incidence. On the contrary, Van Staa *et al*.[14]. concluded that the use of ICS in asthmatic children was associated with a 15% increased risk in fractures. Unlike this study, all above mentioned studies did not include any information regarding smoking status, environmental smoke exposure and activity levels, limiting their ability to control for those confounders in their analyses. In a retrospective cohort study with 40-year follow up Melton *et al*.[12] investigated fracture risk in asthmatic children without accounting for ICS use. This study indicated that there was no increase in overall fracture risk in children; however, due to the long follow up, these fractures cannot be directly linked to ICS use.

This study did also show that bone health parameters such as adequate calcium and vitamin D supplementation was extremely low (<10% in each sub-group) across the whole study population even though the majority of participants were taking less than the daily recommended calcium intake. Although BMD measurements were out of the scope of this study, hopefully this study still raises awareness that there is room for just the simple recommendation of increasing the uptake of calcium and vitamin D supplementation in paediatrics to improve bone health as a first point of call.

The dental department at the RCH, where the control participants were recruited, is attended by children from lower socioeconomic regions; socio-demographic status has been linked to fracture risk[21]; this may have increased the fracture rate in our healthy control population but due to the anonymous nature of our survey, it is not possible to know to what extent socioeconomic status affected our population.

Although this study used a questionnaire to collect data increasing the risk of recall bias, the vast majority of the questionnaires were filled out either by one of the parents/guardian or by the child with the parent/guardian alongside them and it is unlikely a child's fracture would have been forgotten. Questionnaires were researcher administered to reduce the likelihood of misinterpretation of questions and missing data. Due to the design of the survey, a great variety of information regarding possible risk factors such as BMI, daily calcium intake, history of bone health supplement use, smoking and exposure to household smoking, activity levels and in-depth information regarding asthma history and asthma control was able to be captured for each study participant. This enabled us to perform extensive analysis on the association between ICS use in asthmatic patients and fracture risk factors. This was particularly useful here as recent studies have shown BMI to be associated both with the severity of asthma symptoms,[22] as well as an increased risk of fractures in general.[23]

Further research should be performed to investigate prospective, long-term follow up into adult life in conjunction with assessment of ICS adherence and persistence using objective measures and assessment of inhaler techniques. It is important that the impact of ICS on bone health in asthmatic children be extensively examined since fractures can cause severe disability and reduce quality of life.[24-25] With the use of techniques like peripheral quantitative computed tomography (pQCT), early changes in bone metabolism and corticosteroid-induced osteoporosis may be monitored and earlier intervention could be implemented to improve bone health in asthmatic children, if warranted.

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