REFERENCES

1. Omalizumab SmPC. <https://www.medicines.org.uk/emc/medicine/24912>
2. NICE Guidance 278. <https://www.nice.org.uk/guidance/ta278>

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A SYSTEMATIC REVIEW AND META-ANALYSIS FOR THE ASSOCIATION OF PARACETAMOL AND CHILDHOOD ASTHMA: BREATHING NEW LIFE INTO AN OLD MYTH?

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Introduction and Objectives Paracetamol is globally the most frequently prescribed drug amongst infants being employed in a variety of different contexts – from acute febrile illnesses to postoperative analgesia. Prior epidemiological evidence had long inferred a correlation between paracetamol to the ontogeny and exacerbation of asthmatic symptoms, leading to some clinicians advocating for a total prohibition. In view of the evidence being primarily from cohort studies, uncertainty persisted about the strength of the evidence as concerns were raised about the validity of observational cohort studies to ascertain causation, particularly in the absence of a placebo or a control group.

Methods A systematic review of the medical literature search was performed from bibliographic databases that included: Pubmed/Medline, EMBASE, CINAHL, CENTRAL, and Google Scholar; from 1975 until June 2017, using a prospective and explicit search criteria. The Mantel Haenszel (MH) method using a random effects model calculated the weighted odd ratio (OR).

Results 256 studies were identified from abstracts and titles with 9 studies being included in this review: 7 were prospective cohorts studies and two RCTs. The study ascertained that paracetamol was not associated with increased risk of asthma symptoms: MH-OR 0.083 (95% CI 0.051–0.1332). However,

the substantially high degree of heterogeneity ($I^2=99\%$) illustrated the limitations of combining the weighted MH-OR from cohort studies. Four prospective cohort studies reported a statically significant association between paracetamol and asthma symptoms, whereas a well conducted, rigorous, double blinded RCT found no significant difference. The potential mechanisms by which paracetamol induced bronchospasm has not been fully elucidated; however the depletion of glutathione in lung parenchyma, increased intra and extra-mitochondrial oxidative stress, and reactive oxygen species are all thought to have a contributory role.

Conclusions Whilst prior cohort studies had previously inferred causation between paracetamol and the exacerbations of asthma symptoms, a well conducted and rigorous RCT demonstrated no significant association. Notwithstanding the limitations of meta-analysis, we recommend that paracetamol remains safe, with usage being contextualised to follow current best practice paradigms. Reflectively, the review raises the caveat of the unquestioned advocacy of paracetamol or any drug as a cultural axiom.

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IDENTIFYING THE CHILD (5–12 YEARS) WITH ASTHMA AT INCREASED RISK OF ATTACKS: THE AT-RISK CHILD WITH ASTHMA (ARC) SYSTEMATIC REVIEW

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Introduction and Objectives Asthma is the commonest long-term condition in children with attacks impacting on both

Abstract S61 Figure 1 Summary of the included studies, a forest plot for random effects meta-analysis of odd ratios and summary of the risk of bias.

school attendance and quality of life. Identifying the child at increased risk of future asthma attacks could inform clinical management and targeting of care. We aimed to systematically review the literature to identify and weight factors associated with increased risk of attacks in children with asthma aged 5–12 years.

Methods Using Cochrane methodology, we systematically searched six databases and undertook forward and backward citation searches, with no date/language restrictions. Two reviewers independently selected studies for inclusion, assessed methodological quality, and extracted data. An expert panel of four clinicians independently assessed each factor for both magnitude of risk and degree of confidence in that assessment, based on study quality, effect sizes, biological plausibility, and consistency of Results Consensus was achieved by discussion and agreed at a multidisciplinary workshop.

Results From 16 109 records, we included 69 papers (29 cohort, 4 case-control, 36 cross-sectional studies) providing data on 32 potential factors associated with an increased risk of asthma attacks. The panel had high confidence that previous asthma attacks were associated with greatly increased risk of future attacks. Poor access to care and persistent symptoms were associated with moderately/greatly increased risk. A moderately increased risk of attack was associated with sub-optimal drug regimen (low controller/total therapy ratio), comorbid atopic/allergic disease, African-American ethnicity (US studies), poverty, and vitamin D deficiency. Environmental tobacco smoke (ETS) exposure, younger age, and obesity were associated with slightly increased risk. Gender, urban residence, and Hispanic ethnicity (US studies) were not associated with risk. The evidence for other factors was inconclusive.

Conclusions Assessment of clinical and demographic features (especially persistent symptoms, previous attacks, and sub-optimal drug regimen) may help clinicians to ‘spot the child’ at increased risk of asthma attacks and focus appropriate management. Population level factors (poverty, poor access to care) may be used by health service planners and policymakers to target healthcare initiatives.

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DO THE ROYAL COLLEGE OF PHYSICIANS ‘THREE QUESTIONS’ PREDICT SYMPTOM CONTROL IN PAEDIATRIC ASTHMA?

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Introduction and Objectives The UK Quality Outcomes Framework (QOF) rewards primary-care practices for completing the Royal College of Physicians “Three Questions” (RCP3Q) score for all patients listed on their asthma register. Almost no validation data currently exists, however, to support its use in

children. This study aimed to investigate the performance of the RCP3Q to predict asthma control in children, by comparing it with the validated Asthma Control Test (ACT) or Childhood Asthma Control Test (C-ACT).

Methods This was a prospective, observational study involving 8 primary-care practices. Children aged 5–16 on the QOF asthma register and/or receiving asthma medication were invited to self-complete the ACT (age 12–16, n=96) or C-ACT (age 5–11, n=223) questionnaire immediately prior to a primary-care asthma review, where responses to the RCP3Q were collected. RCP3Q scores were compared with ACT or C-ACT data to assess performance of the RCP3Q in predicting asthma control. The RCP3Q scoring system is summarised in figure 1.

Results Questionnaire and RCP3Q data was completed for 319 participants. RCP3Q scores correlated moderately with C-ACT and ACT data (Spearman’s rho –0.49 and –0.52 respectively, $p < 0.001$). A RCP3Q score of ≥ 2 predicted uncontrolled asthma (C-ACT or ACT ≤ 19) with a sensitivity of 57% and specificity of 81%. A lower threshold RCP3Q score of ≥ 1 gave a specificity of 55%, resulting in a high false positive rate. A RCP3Q score of 0 predicted well-controlled asthma (C-ACT or ACT ≥ 20) with a sensitivity of 55% and specificity of 81%. Using thresholds of RCP3Q ≥ 2 for uncontrolled asthma and RCP3Q = 0 for good control resulted in 25% participants unclassified (RCP3Q = 1) and 18% of participants scoring 0, 2 or 3 incorrectly classified. Binary logistic regression showed that individual positive answers to RCP questions 1 and 2, but not 3, significantly increased the likelihood of uncontrolled asthma.

Conclusions Our data in ≥ 300 participants does not support use of the RCP3Q to classify asthma control in children. Our findings support current BTS/SIGN guidelines, which recommend use of validated asthma control questionnaires, such as C-ACT, when conducting a paediatric asthma review.

Asthma: infection and inflammation

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CLINICAL AND TRANSCRIPTOMIC PROFILES OF SEVERE ASTHMATICS WITH HIGH OR LOW EXPRESSION OF THE GLUCOCORTICOID RECEPTOR AND IMPORTIN-7

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Introduction and Objectives The majority of asthmatics can be well-controlled using inhaled corticosteroids (ICS) and long-acting β_2 -agonists (LABAs). However, approximately 5% have a severe, refractory form of the disease and are often difficult to treat. Corticosteroid (CS) Insensitivity is the defining feature of these asthmatics known as “severe” asthmatics. The

In the last month:

1. Have you had difficulty sleeping because of your asthma symptoms (including cough)?
2. Have you had your usual asthma symptoms during the day (cough, wheeze, chest tightness or breathlessness)?
3. Has your asthma interfered with your usual activities (e.g. housework, work, school etc)?

Score 1 for each yes answer, with total score ranging from 0 and 3.

Abstract S63 Figure 1