Biomarkers in Adult Asthma: A Systematic Review of 8-Isoprostane in Exhaled Breath Condensate

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Introduction The potential of exhaled breath condensate (EBC) as a non-invasive indicator of airways disease has been studied for three decades or more. 8-isoprostane is a product of lipid peroxidation which can be detected within EBC. Studies have reported this as a potential objective indicator of oxidative stress in asthma. We therefore aimed to assess the evidence for the use of 8-isoprostane in exhaled breath condensate (EBC) as a biomarker in adult asthma.

Design A systematic review and meta-analysis of EBC 8-isoprostane in asthma.

Methods We searched a number of online databases (including PubMed, Embase and Scopus) in January 2016. We included studies of adult non-smokers with EBC collection and asthma diagnosis conducted according to recognised guidelines. We aimed to pool data using random effects meta-analysis and assess heterogeneity using I2. Study quality and risk of bias was assessed using QUADAS-2 and GRADE.

Results We included twenty studies, the findings from which were inconsistent. Seven studies (n = 329) reported 8-isoprostane concentrations in asthma to be significantly higher than that of control groups, whilst six studies (n = 403) did not. Only four studies had results appropriate for inclusion in a random effects meta-analysis of mean difference between asthma and controls (see Figure 1). This found a statistically significant between-groups difference of +22 pg/ml in asthma.

Confidence in the result is limited by the small number of studies; by substantial methodological and statistical heterogeneity (I^2 = 94); and by an inability to assess the risk of bias in key domains of the quality assessment tool.

Conclusion The clinical value of EBC 8-isoprostane as a quantitative assessment of oxidative stress in asthma remains unclear due to variability in results and methodological heterogeneity. It will be essential to develop accurate, reliable and standardised methods of both EBC collection and 8-isoprostane analysis if its use as a biomarker in asthma is to be evaluated.

Abstract S1 Figure 1 Random effects meta-analysis of mean between-group difference (asthma vs controls)
Background Severe asthma comprises 5% of all asthma, but over 50% of the asthma healthcare burden. With a multidisciplinary team (MDT) working there is potential to improve patient outcomes and reduce healthcare costs. In 2013 NHS England produced service specifications for severe asthma aiming to develop a limited number of high volume specialist centres. In the North West we have developed a networked approach to specialist severe asthma services; the first Operation Delivery Network for asthma MDT working there is potential to improve patient outcomes. Representatives from 11 NHS Trusts and a central hub undertake a monthly virtual MDT meeting, with physicians, nurses, physiotherapists, clinical psychologists, speech and language therapists, allergists, pathologists and radiologists represented. All patients being considered for specialised treatments undergo MDT discussion for consensus approval of treatment.

Aim To summarise the experience and case-mix encountered during the first 18 months of operation of our regional virtual severe asthma MDT

Methods We reviewed all cases discussed at the MDT between January 2015 and June 2016. Cases were submitted online via nhs.net accounts, and data entered into a central database managed by two MDT coordinators for MDT discussion.

Results During this period 17 meetings were held, with 208 case-submissions representing 185 patients, mean (SD) 12 (7) discussions per meeting. Indications for case submission included proposals for use of omalizumab, bronchial thermoplasty (BT), and steroid-sparing therapies, and for the discussion of patients with complex clinical issues, often managed across multiple sites. Omalizumab was approved in 81% of cases submitted, and BT in 39%, with more of the latter requiring multiple discussions (30% versus 2%). The most common reasons for non-approval of omalizumab were insufficient steroid requirement, poor adherence, and lack of allergy to a perennial allergen. Thermoplasty was not approved or listed for re-discussion for a variety of reasons, including 10 (43%) that required further investigation.

Conclusion We describe our early experience of a multi-site virtual severe asthma MDT meeting facilitating expert care across a wide geographical area. This ensures governance in the use of novel and expensive severe asthma therapies, strengthens regional collaborations and ultimately aims to provide better patient care.