Discussion Despite limitations of included studies, the prevalence of silicosis and TB appears high which is likely due to RCS exposures between 4–1790 times above the US permissible exposure limit. Our modelling demonstrated the greatest respiratory health benefits of reducing RCS are in those with the highest exposures. Effective low-cost interventions are available and should be studied and implemented.

### IMPACT OF TYRE AND ROAD WEAR PARTICLES (TRWPS) ON HUMAN RHINOVIRUS INFECTION IN HUMAN AIRWAY EPITHELIAL CELLS

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**Background** Air pollution by car emission is known to cause detrimental respiratory effects, especially on vulnerable populations, such as children and individuals with underlying chronic respiratory diseases, including asthma and chronic obstructive pulmonary disease (COPD). An increasing number of vehicles on the road has been reported to result in high levels of TRWPs being released due to their heavy weight. Despite this, little research has explored the effect of TRWPs on respiratory systems. In this study, we investigated effects of TRWPs on cell damage and human rhinovirus infection, which is a major cause of exacerbation of asthma and COPD, in human bronchial epithelial cells.

**Methods** Immortalised human bronchial epithelial cells, HBEC3-KT, were treated with N-cyclohexyl-1,3-benzothiazole-2-amine (NCBA), N-(1,3-dimethylbutyl)-N’-phenyl-p-phenylenediamine (6-PPD), 1,3-diphenylguanidine (DPG), 2,4-morpholinyl-benzothiazole (24MoBT), 1,3-butadiene, 2-methylbutadiene (2-MB), DL-limonene, and styrene/butadiene copolymer, and cell toxicity was determined using resazurin assay.

Cells were also exposed to selected TRWP concentrations prior to human rhinovirus (HRV16) infection, and viral load was assessed using a 50% tissue culture infectious dose (TCID\(_{50}\)) assay.

**Results** NCBA and 6-PPD (100\(\mu\)g/ml) significantly decreased cell viability (6.87% of control (\(p=0.0412, N=3\)) and 5.94% (\(p=0.0054, N=3\)) viable cells respectively) although other chemicals showed no or little impact on cell viability up to 100\(\mu\)g/ml. In addition, NCBA and 1,3-butadiene (both, 0.1\(\mu\)g/ml) generated 2.2 and 4.3 fold higher viral load compared to their respective controls, respectively. In addition, 2-methylbutadiene (2-MB) (10\(\mu\)g/ml) was found to delay HRV16 clearance as viral load remained higher than control on Day 5.

**Conclusion** Some TRWPs were found to cause cell damage or increased rhinovirus infection in HBEC3-KT cells. These findings provide us with an important insight as to how TRWPs affect our respiratory health, and what solutions may be implemented in the future to reduce TRWP emissions from vehicles and help abate the health impacts of TRWPs to improve public health. The observations in this study indicate that future investigation and study is highly warranted.
The London Underground (LU) employs over 19,000 staff, some of which are exposed to elevated concentrations of particulate matter (PM) due to emissions within the network. Little is known about the health effects of this PM, which can reach concentrations 15 times higher than outdoor PM and is different in both chemical and physical composition. The aim of this study was to quantify the occupational exposure of LU staff to PM and investigate whether these elevated exposures were associated with increased cardiorespiratory sickness absence.

A job exposure matrix was developed to quantify the exposure of LU staff to PM based on their activity during the working day by undertaking personal and static measurement campaigns across the LU network. The 29,744 staff were grouped into distinct exposure groups, which were linked to sickness absence records (2014–2019). The association between exposure and sickness absence was evaluated using zero-inflated mixed effect negative binomial models.

Staff PM exposure varied by job grade and tasks undertaken. Drivers had the highest exposure over a work shift (median: 130 μg/m³), but levels varied significantly by the line on which they worked and the duration of time the train spent underground.

All non-office-based staff had significantly higher rates of all-cause and respiratory infection sickness absence. When looking at drivers only, five out of eight lines had significantly increased rates of all-cause sickness absence, however no dose response relationship was seen. Only drivers on the Central line had significantly higher rates of sickness absence from respiratory infections (incidence rate ratio (IRR): 1.24, 95% CI 1.10, 1.39). Chronic respiratory and cardiovascular sickness absence records (2014–2019). The association between exposure and sickness absence was evaluated using zero-inflated mixed effect negative binomial models.

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While staff with higher occupational exposure to subway PM reported higher rates of sickness absence in some cases, there was no conclusive evidence to suggest that LU PM is the sole contributing factor to sickness absence. This is the largest study to quantify PM exposure and the associated health effects within a London occupational cohort to-date and may have wider implications for the LU workforce that can contribute to a safer working environment for staff.

Please refer to page A284 for declarations of interest related to this abstract.

‘It’s complicated’ – Answering the unanswered in asthma biologics

**S62**

**WATCHING AND WAITING: OUTCOMES AMONG PATIENTS WITH SEVERE ASThma DEMONSTRATING PARTIAL RESPONSE TO MONOCLonal ANTIBODY THERAPY OVER 2 YEARS**

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**Introduction** Super-response (SR), defined as a cessation of oral corticosteroid (OCS) therapy and elimination of exacerbation, is a key treatment goal among patients with severe asthma (SA) on monoclonal antibody (mAb) therapy. Key predictors of SR remain elusive, and delayed SR (post 12-months’ therapy) has not been well described. We explore long-term outcomes among patients with SA demonstrating partial response (PR) – ≥ 50% and <100% reduction in maintenance OCS and/or courses of OCS – to mAb therapy at 12 months.

**Methods** Retrospective analysis of patients with physician-confirmed SA commenced on mAb therapy from January 2019 – May 2021 who demonstrated PR at 12 months. We assessed baseline characteristics, clinical outcomes at 12 and 24 months, and treatment decisions. A subgroup analysis compared those who maintained PR at 24 months with those who went on to develop SR.

**Result** 194 patients were started on mAb therapy, of whom 72.7% (n=141; Benralizumab = 86, Mepolizumab = 31, Omalizumab = 19, Dupilumab = 5) demonstrated PR at 12 months. Among this group, clinical outcomes, including OCS use, annualised exacerbation rate (AER), Asthma Control Questionnaire (ACQ-6) and mini Asthma Quality of Life Questionnaire (mAQLQ) were not significantly different between 12 and 24 months’ therapy.

Within this cohort, 121 (85.8%) maintained PR at 24 months’ therapy, with 20 (14.2%) developing SR. There were no significant differences in baseline demographics or baseline clinical outcomes between the two groups. At 12 months’ therapy, those who went on to develop SR had a significantly improved AER and ACQ-6 compared to those who did not.

At their 24 month review, 60% (n=116) continued on the mAb, 1% (n=2) switched to a new mAb, and 12% (n=23) discontinued treatment.

**Conclusion** Patients who demonstrate partial response to mAb treatment at 12 months may go on to develop super-response by 24 months. Patients who did develop super-response at 24 months had significantly improved AER and ACQ-6 at 12 months compared to those who didn’t, suggesting these may be key criteria to decide whether to continue or switch mAb treatment in patients with partial response.

**S63**

**LONG-TERM EFFECTIVENESS OF ANTI-IL4R THERAPY FOLLOWING SUBOPTIMAL RESPONSE TO ANTI-IL5/5R THERAPY IN SEVERE EOSINOPHILIC ASTHMA**


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**Introduction** Dupilumab is an anti-IL4R monoclonal antibody (mAb) with proven efficacy in severe eosinophilic asthma (SEA). A suboptimal response to the eosinophil-targeting anti-IL5/5R mAbs mepolizumab and benralizumab is seen in ~20% of patients with SEA. We have previously reported that a significantly improved response in this cohort is seen following 6 months of treatment with dupilumab. It is unknown whether this response is maintained in the long-term.

**Methods** We performed a retrospective analysis of the clinical effectiveness of dupilumab at 1 year and 2 years of treatment in patients with SEA who had not responded adequately to anti-IL5/5R biologics. Change in the exacerbation rate (AER), maintenance oral corticosteroid dose (mOCS), lung function (FEV1) and change in symptom scores (ACQ6 and mAQLQ) were recorded.