# Health effects from combustion ultrafine particles: consistent observations from controlled human exposure studies

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The human health effects from exposure to ultrafine particles are challenging to assess. The exposure has complex spatial, temporal, multi-source and co-pollutant variables and the health indicators have multiple etiologies, besides the inter-individual variation in susceptibility. Controlled human exposure studies are a particular study design that allows investigating short-term effects from combustion particles, consisting of experiments where human volunteers agree to be intentionally exposed to pollutants, in a controlled short-term scenario, to provide information on biological changes caused by the exposure. These studies are usually performed in an exposure chamber with controlled air composition, ventilation, temperature, and humidity conditions. Particles are generated by combustion and/or concentration processes or resuspension, and forced into the chamber also allowing the control of mixtures and co-exposures. We revisited the strengths and limitations of this study design and reviewed and compared 64 controlled exposure studies following exposure of a total of 1338 healthy, non-smoking subjects to combustion-generated particles, including 12 chamber studies on wood smoke, 33 on diesel exhaust, 15 on concentrated ambient particles and 4 on indoor carbonaceous sources (candle burning, cooking and printing). Besides different combustion source and generation conditions for the same source, the studies differ by design (crossover or sequential), protocol definitions (with or without moderate physical activity), administrated doses and duration of exposure, as well as the assessed biomarkers and functional markers and methods used in the assessment. The most common markers assessed were inflammation, vascular function and lung function, with less studies focusing on neurotoxicity, arrhythmia and genotoxicity. Consistency of effects (observed in ≥75% of the studies from the same source and involving more than 50 study subjects) were observed after exposure to concentrated ambient particles (vascular function, heart rate variability, arrhythmia and oxidative stress) and diesel exhaust (airway inflammation and vascular function).

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