Supplementary Information:

Effects of breathing variables on modelled particle lung deposition at physical activity for children and adults

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References for the alteration of breathing variables at increasing physical activity

The collected data from previous research studies on the alteration of tidal volume (V_t) with increasing minute ventilation (V_e) is presented with references in Fig. S1. The data from Lind and Hesser was not included in the polynomial fit for the adult data due to that it disagreed with the other studies (Fig. S1a).

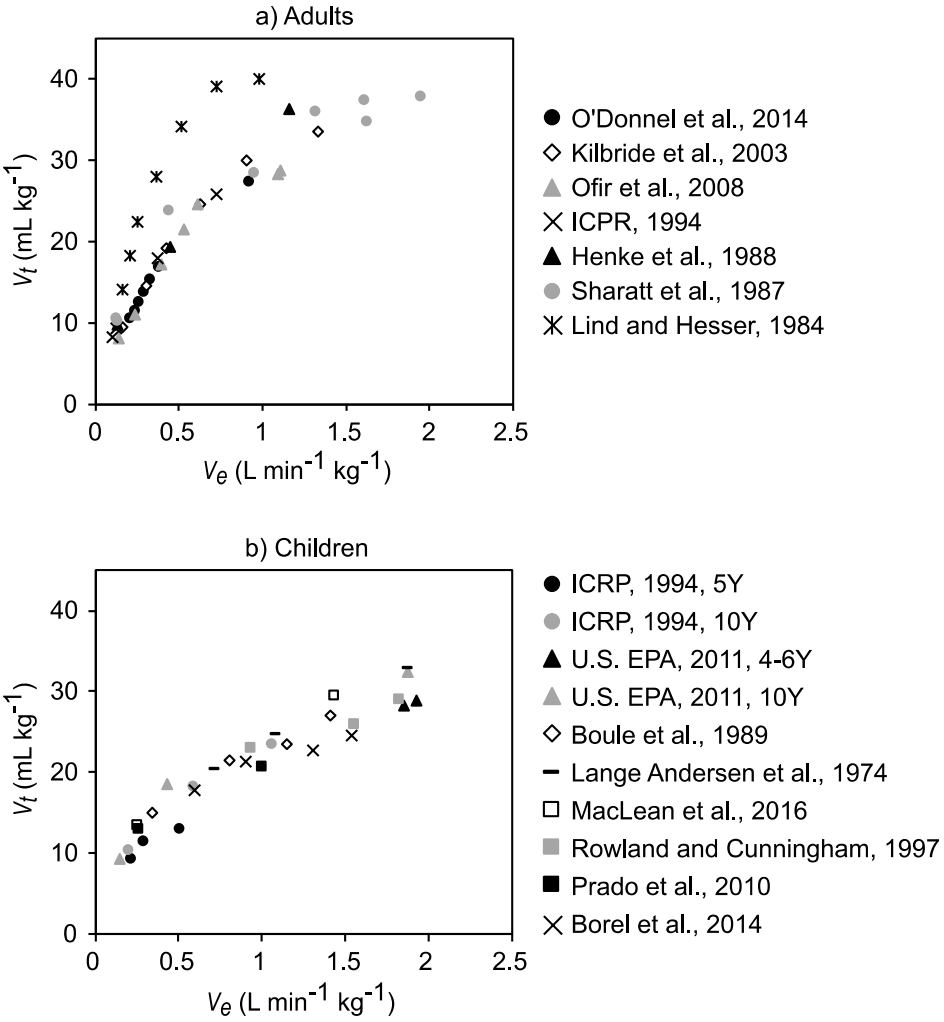

Fig. S1. Results from the literature review on the alteration of tidal volume (V_t) with increasing minute ventilation (V_e) for a) adults and b) children.

Nasal contribution to breathing

Bennett *et al.* (2008) measured total (corresponding to V_e) and nasal ventilation and present percent nasal contribution to breathing at different physical work capacities in adults and children (6–10 years old). The measured V_e ranges were 8–33 L min^{-1} for adults and 7–22 L min^{-1} for children. Linear regressions were made between V_e and percent nasal contribution (Fig. S2) for the data. These equations were used to estimate the nasal contribution to breathing for the V_e used in the current study.

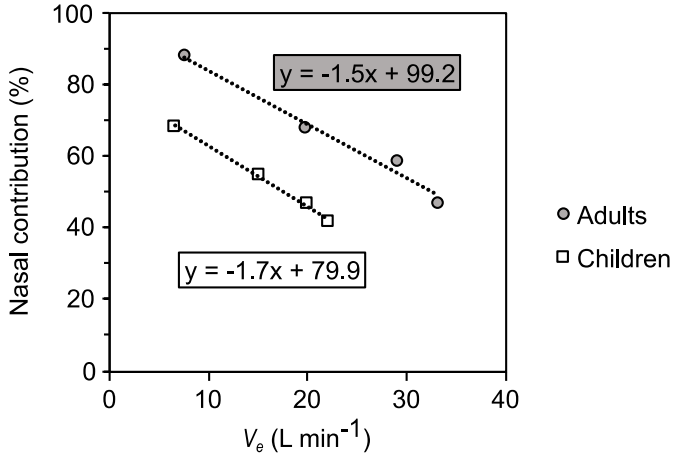

Fig. S2. Linear regressions for nasal contribution to breathing at different minute ventilations (V_e) for adults and children (6–10 years old). The data originates from Bennett *et al*. (2008).

Particle data for dose estimations

For the urban example number size distribution, data from a custom built DMPS (details in (Krecl et al., 2017) for the size range 9–453 nm and an OPC (GRIMM, model EDM 180) for the size range 0.25–32 µm was obtained from Hornsgatan in Stockholm, Sweden. For the rural example number size distribution, data from a MPSS/DMPS (Hauke type DMAs and UCPC/CPC from TSI3025/TSI3772) for the size range 3–926 nm and an OPC (PalasFIDAS 200S) for the size range 0.1–27 µm was obtained from the rural background stations Hyltemossa and Hallahus, respectively, both located in southern Sweden. The size distributions were averaged (mean) over two years (2017–2018 for the urban site and 2018–2019 for the rural sites). The data coverage was 73% for DMPS and 96% for GRIMM OPC at the urban site, while 81% for MPSS/DMPS and 78% for PalasFIDAS OPC at the rural sites. The data were converted to mass size distributions by assuming spherical particles and a density of 1 g cm^{-3}.

Since the OPCs measure the optical particle diameter, the diameters were transformed to aerodynamic diameters using equations presented in Chien *et al*. (2016). The aerodynamic diameters were calculated using both the equation for oleic acid and sodium chloride, and averages between them were calculated for the final aerodynamic diameters. Since our data represents ambient aerosols (not homogenous as in Chien *et al*.) the estimated doses are to be viewed and treated as examples and not actual doses.

The final diameter intervals used to estimate deposited doses were 0.01–0.34 µm and 0.53–5.4 µm for the urban DMPS and GRIMM OPC, respectively; and 0.01–0.86 µm and 0.89–5.2 µm for the rural MPSS/DMPS and PalasFIDAS OPC, respectively. The final particle size distributions are presented in Fig. S3.

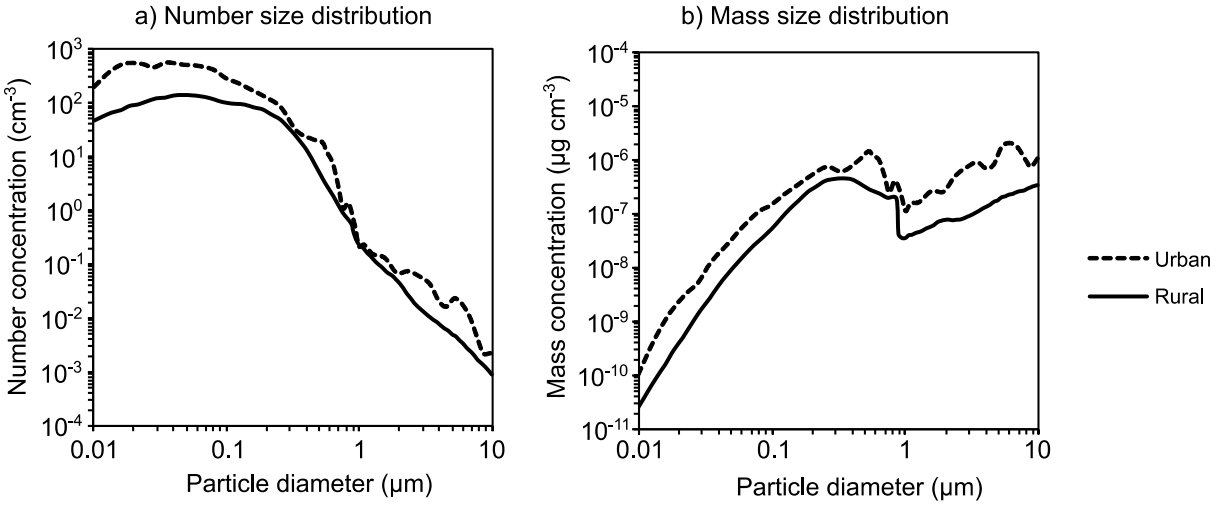

Fig. S3. Final a) number size distributions and b) mass size distributions for the urban example site Hornsgatan in Stockholm, Sweden, and the rural background stations Hyltemossa and Hallahus, Sweden.

Regional deposited fraction for children at increasing activity

The regional deposited fractions for three particle size intervals in children at increasing activity are shown in Fig. S4.

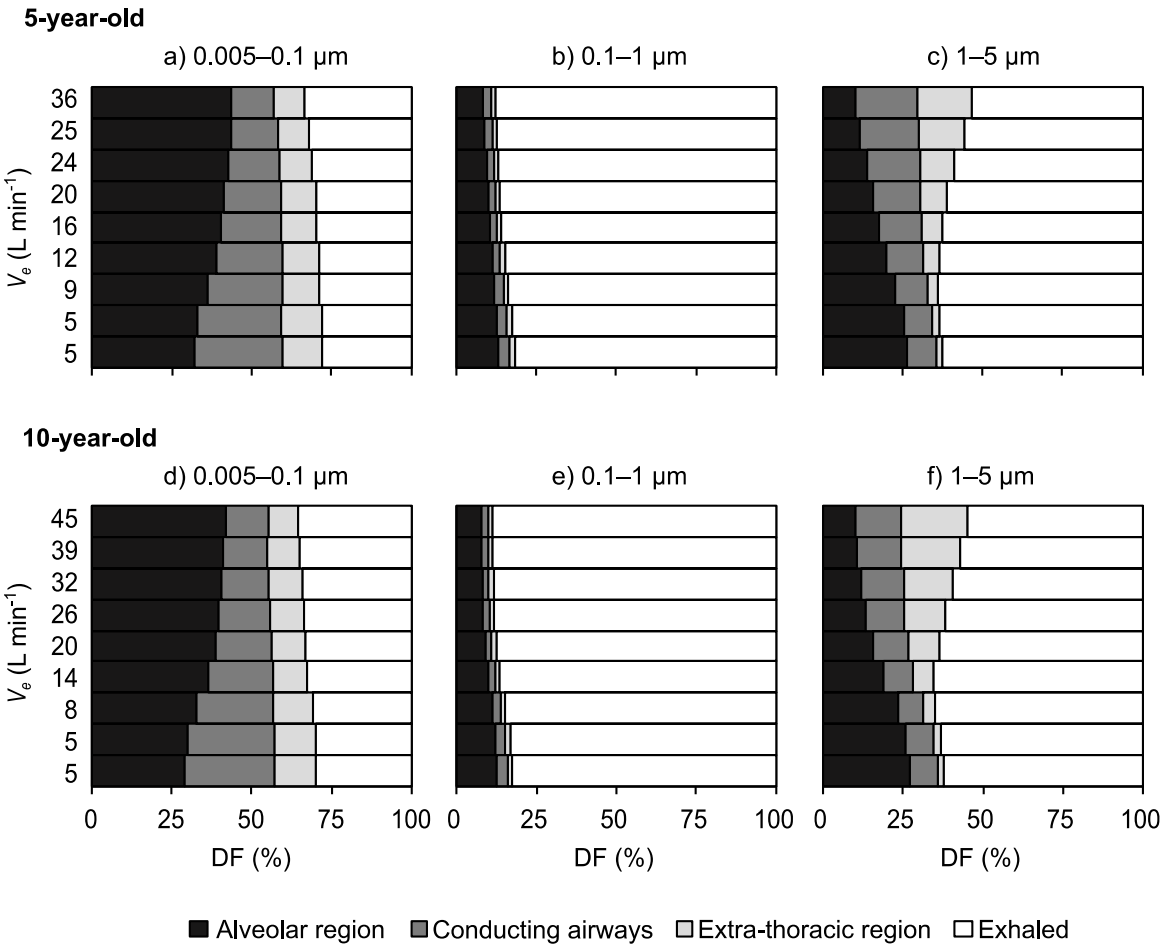

Fig. S4. Deposited fractions (DF) of particles in the three regions of the respiratory tract as well as the exhaled fraction at increasing minute ventilation (V_e) expressed as mean values in three size ranges for a–c) 5-year-olds and d–f) 10-year-olds. The modelling was performed for oral breathing.

Deposition mechanisms

Size resolved DF separated to show the relative contribution from different deposition mechanisms are shown in Fig. S5. The curves were generated for four V_e corresponding to rest, light, moderate and high intensity physical activity (see Table 2 in the main text) for adults. It should be noted that the impaction increased more with physical activity for the two groups of children than what is indicated by the example with the adult group.

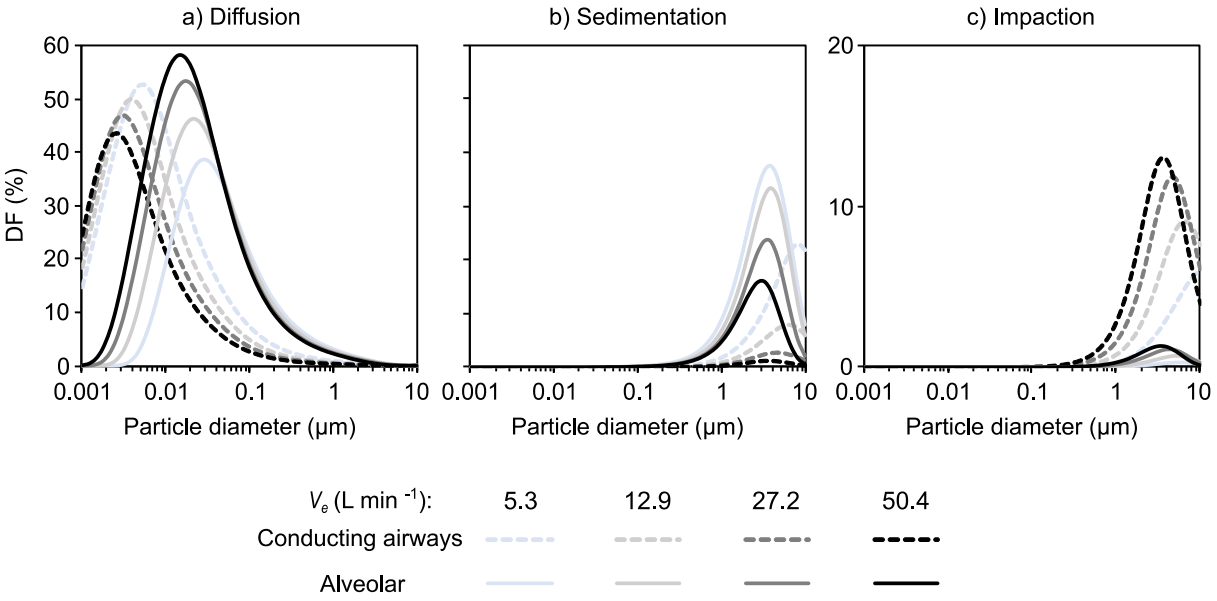

Fig. S5. Deposited fraction (DF) due to a) diffusion, b) sedimentation and c) impaction (note the axis) in the conducting airways and alveolar region for the adult group. The modelling was performed for oral breathing and constant functional residual capacity (3100 mL).

Nasal deposition

Nasal breathing resulted in an increased total DF of particles > 0.1 µm compared to oral breathing in adults (Fig. S6), due to increased deposition by impaction in the nasal passage and pharynx (extra-thoracic region). In line with this, DF was decreased in the alveolar region for particles > 1 µm and < 0.01 µm due to that fewer of them reach the deeper lung compared to when breathing orally. The decreased difference in the alveolar region for the higher V_e (≥ 22 L min^{-1}) compared to the lower V_e is due to that DF decrease for both nasal and oral breathing and thus the difference between them is smaller. Similar patterns were seen for the two groups of children.

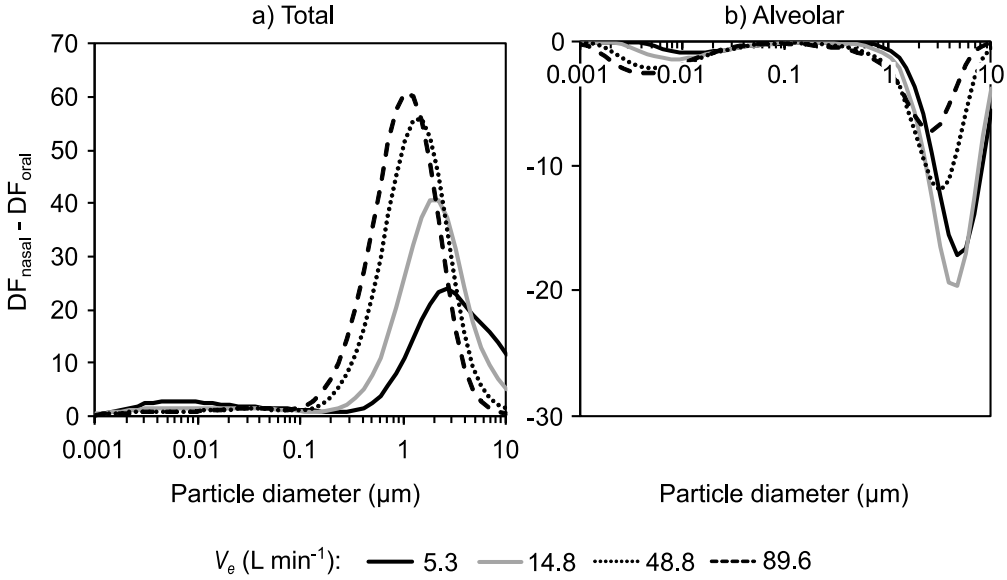

Fig. S6. Difference in the deposited fraction (DF) of particles between nasal and oral breathing in a) the entire respiratory tract (total) and b) alveolar region. The modelling was performed for a constant functional residual capacity (3100 mL).

Fit to size resolved deposited fractions

Table S1 shows the sum of residuals (difference between data and the fit) for the parametrizations of the daily average size resolved DFs (0.005–5 µm) in the entire respiratory tract (total) and alveolar region. The fit to the daily average size resolved alveolar DF can be seen in Fig. S7, note that the parametrizations fit best for particles < 0.1 µm.

Table S1. Sum of residuals for the fit to the alveolar and total daily average size resolved deposited fraction.

	Total	Alveolar
5-year-old	0.006	0.013
10-year-old	0.004	0.013
Adult	0.006	0.012

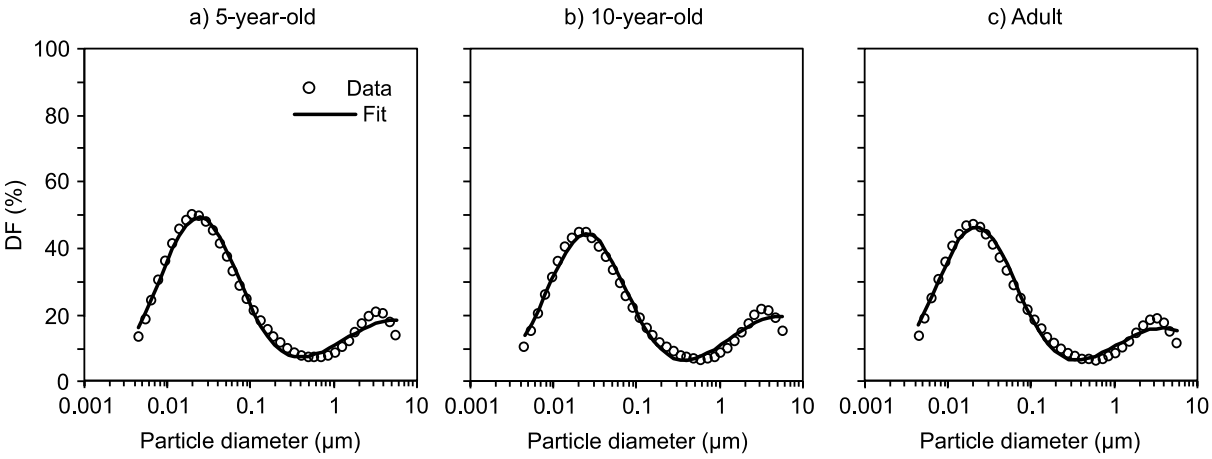

Fig. S7. Data and fit to the daily average size resolved deposited fractions (DF) (0.005–5 µm) for a) 5-year-olds, b) 10-year-olds and c) adults.

Parametrizations of the size resolved DF for all four physical activity levels are presented in Tables S2 and S3. Note that the parametrizations of the size resolved total DF fit better for the lower activity levels compared to high intensity activity. The parametrizations of the size resolved alveolar DF was best for particles < 0.1 µm for all physical activity levels.

Table S2. Values of constants from the least square fit of the size resolved deposited fractions of 0.005–5 µm particles in the entire respiratory tract for rest, light, moderate and high intensity physical activity.

	A	**B**	**C**	**D**	**E**	**Sum of residuals**
Rest						
5-year-old	0.936	0.307	0.168	0.026	1.417	0.009
10-year-old	0.928	0.317	0.174	0.027	1.378	0.009
Adult	0.922	0.362	0.193	0.025	1.369	0.010
Light activity						
5-year-old	0.953	0.335	0.182	0.014	1.520	0.007
10-year-old	0.938	0.335	0.183	0.017	1.431	0.005
Adult	0.943	0.403	0.212	0.015	1.472	0.011
Moderate activity						
5-year-old	0.970	0.337	0.184	0.010	1.565	0.006
10-year-old	0.965	0.317	0.175	0.010	1.505	0.005
Adult	0.975	0.382	0.206	0.009	1.533	0.010

High intensity activity						
5-year-old	0.952	0.261	0.135	0.009	1.556	0.034
10-year-old	0.952	0.232	0.116	0.009	1.525	0.033
Adult	0.953	0.242	0.122	0.009	1.548	0.035

Table S3. Values of constants from the least square fit of the size resolved deposited fractions of 0.005–5 μm particles in the alveolar region for rest, light, moderate and high intensity physical activity.

	F	**G**	**H**	**Sum of residuals**
Rest				
5-year-old				
mode 1	0.515	0.034	2.918	0.019
mode2	0.382	4.77	3.777	
10-year-old				
mode 1	0.469	0.034	2.887	0.019
mode 2	0.341	4.02	3.273	
Adult				
mode 1	0.429	0.035	2.864	0.018
mode 2	0.266	3.035	2.874	
Light activity				
5-year-old				
mode 1	0.593	0.023	2.938	0.014
mode2	0.519	15.24	10.418	
10-year-old				
mode 1	0.535	0.024	2.918	0.014
mode 2	0.478	12.244	7.898	
Adult				
mode 1	0.523	0.025	2.915	0.014
mode 2	0.295	4.498	5.045	
Moderate activity				
5-year-old				
mode 1	0.645	0.019	3.017	0.012
mode2	0.394	12.865	15.542	
10-year-old				
mode 1	0.590	0.019	2.967	0.011
mode 2	0.618	48.144	20.564	
Adult				
mode 1	0.611	0.019	2.978	0.011
mode 2	0.381	10.755	11.551	
High intensity activity				
5-year-old				
mode 1	0.728	0.015	3.230	0.012
mode2	0.185	3.044	5.631	
10-year-old				
mode 1	0.688	0.015	3.174	0.012
mode 2	0.224	4.681	6.717	
Adult				
mode 1	0.747	0.016	3.36	0.014
mode 2	0.180	2.893	3.225	

Daily average deposition curves using results from the Multiple-Path Particle Dosimetry (MPPD©) software

Daily average deposition curves were also created with modelling results from MPPD© v3.04 (Applied Research Associates, Inc., Albuquerque, NM, USA) (Anjilvel and Asgharian, 1995; Miller et al., 2016). In MPPD©, the dimensions of the lungs are constant over time (scaled from the total lung capacity to the functional residual capacity (FRC) + [V_t / 2]) and the deposition is calculated while V_t is moving through the lung airway by airway. The 5-lobe lung anatomy model from Yeh and Schum (1980) was used for adults and the age-specific 5-lobe lung anatomy model for 8 and 9-year-olds (Asgharian et al., 2004; Menache et al., 2008) were used for 5-year-olds and 10-year-olds, respectively.

The age-specific lung anatomies resulted in similar curves for the two groups of children, while the adult curve was different. The deposition for children was higher than adults in the alveolar region over almost the entire size range, for particles > 1µm in the conducting airways and for 0.1–1 µm particles in the extra-thoracic region (Fig. S8).

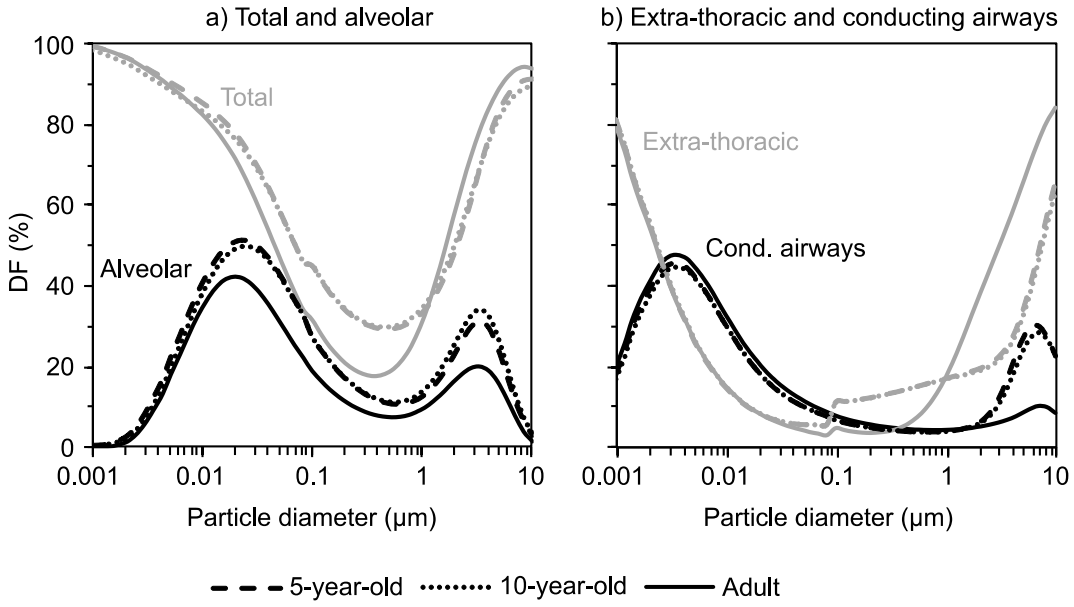

Fig. S8. Daily deposition curves for the three age-groups in a) then entire respiratory tract (total and the alveolar region, and b) the extra-thoracic region and conducting airways.

The major differences of the modelling in MPPD© and the Mimetikos Preludium™ software are

1) the deposition models: MPPD© has its own deposition model while in Mimetikos Preludium™ the NCRP and Yeh and Schum (1980) deposition models were used
2) the scaling of the alveoli: MPPD© scales the alveolar size while Mimetikos Preludium™ adds more alveoli with increasing FRC
3) the airway dimensions: in MPPD© constant airway dimensions are used throughout a breath (scaled to FRC + [V_t / 2]) while in Mimetikos Preludium™ the airway dimensions increase and decrease during a breath (scaled to FRC at full exhalation and FRC + V_t at full inhalation)
4) the lung models: in MPPD© a 5-lobe (asymmetric) lung model was used while a symmetric lung model was used in Mimetikos Preludium™
5) the airflows: a constant airflow is used during inhalation and exhalation in MPPD© while a sinusoidal curve is used to describe the varying airflows during a breath in Mimetikos Preludium™

In comparison to modelling in Mimetikos Preludium™, the MPPD© model showed higher alveolar deposition for children, as well as higher extra-thoracic deposition for particles 0.1–1 µm and higher deposition in the conducting airways for particles > 1 µm. For the adult group both software gave similar results, with MPPD© showing higher deposition for 0.001–0.1 µm particles in the extra-thoracic region and conducting airways, leading to a lower deposition of these in the alveolar region (Fig. S9).

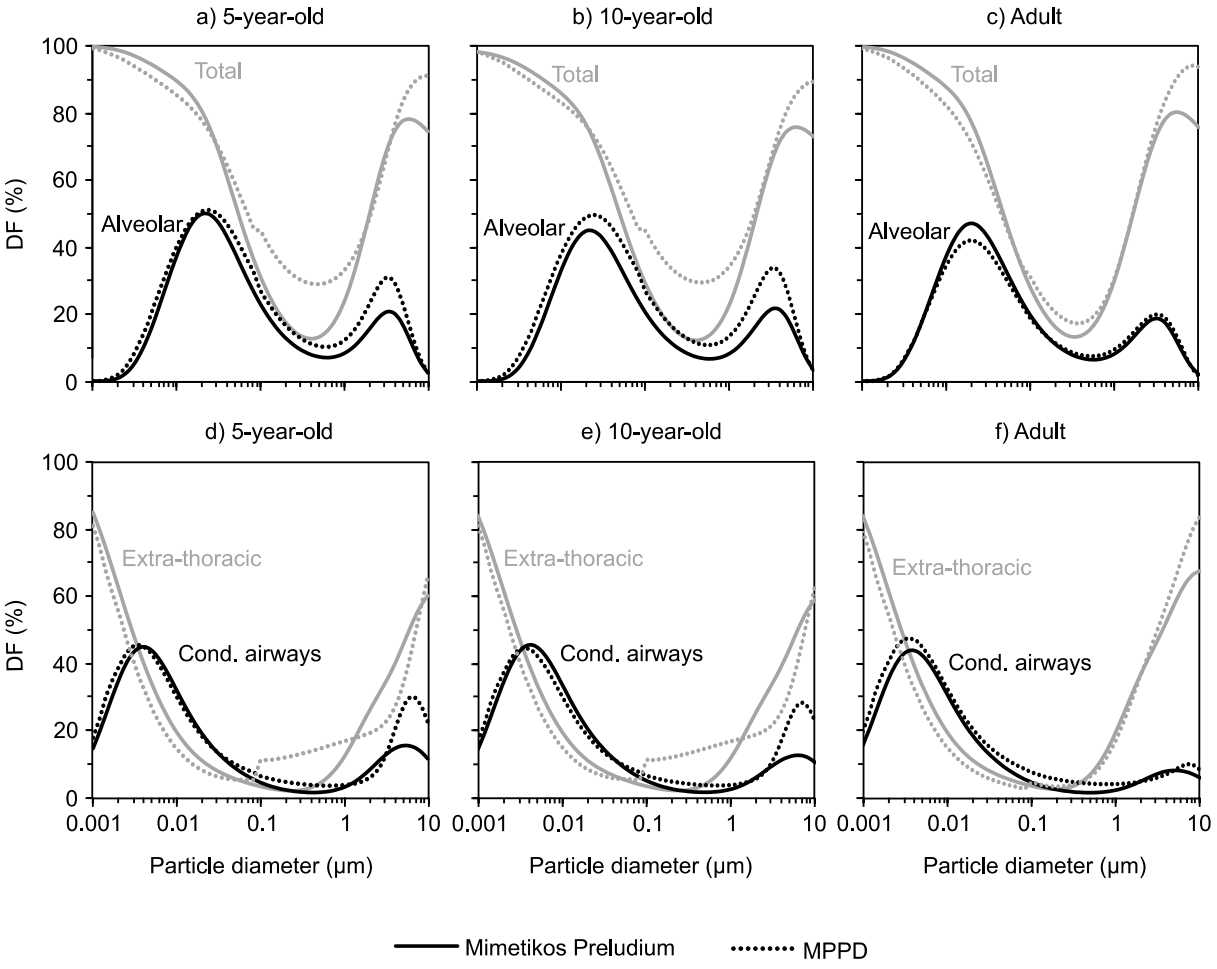

Fig. S9. Comparison of daily deposition average deposited fraction (DF) from modelling in Mimetikos Preludium™ and MPPD© for a, d) 5-year-olds, b, e) 10-year-olds and c, f) adults.

References

Anjilvel S, Asgharian B (1995) A multiple-path model of particle deposition in the rat lung. Fundamental and applied toxicology : official journal of the Society of Toxicology 28:41-50. https://doi.org/10.1006/faat.1995.1144

Asgharian B, Menache MG, Miller FJ (2004) Modeling age-related particle deposition in humans. J Aerosol Med 17:213-224. https://doi.org/10.1089/jam.2004.17.213

Bennett WD, Zeman KL, Jarabek AM (2008) Nasal contribution to breathing and fine particle deposition in children versus adults. J Toxicol Environ Health A 71:227-237. https://doi.org/10.1080/15287390701598200

Borel B, Leclair E, Fabre C, Thevenet D, Beghin L, Gottrand F (2014) Mechanical ventilatory constraints during incremental exercise in healthy and cystic fibrosis children. Pediatr. Pulmonol. 49:221-229. https://doi.org/10.1002/ppul.22804

Boule M, Gaultier C, Girard F (1989) Breathing pattern during exercise in untrained children. Respir Physiol 75:225-233. https://doi.org/10.1016/0034-5687(89)90066-2

Chien CH, Theodore A, Wu CY, Hsu YM, Birky B (2016) Upon correlating diameters measured by optical particle counters and aerodynamic particle sizers. J Aerosol Sci 101:77-85. https://doi.org/10.1016/j.jaerosci.2016.05.011

Henke KG, Sharratt M, Pegelow D, Dempsey JA (1988) Regulation of end-expiratory lung volume during exercise. J Appl Physiol (1985) 64:135-146. https://doi.org/10.1152/jappl.1988.64.1.135

ICRP (1994) Human respiratory tract model for radiological protection. ICRP publication 66. Annals of the ICRP 24

Kilbride E, McLoughlin P, Gallagher CG, Harty HR (2003) Do gender differences exist in the ventilatory response to progressive exercise in males and females of average fitness? Eur J Appl Physiol 89:595-602. https://doi.org/10.1007/s00421-003-0853-z

Krecl P, Johansson C, Targino AC, Strom J, Burman L (2017) Trends in black carbon and size resolved particle number concentrations and vehicle emission factors under real-world conditions. Atmospheric Environment 165:155-168. https://doi.org/10.1016/j.atmosenv.2017.06.036

Lange Andersen K, Seliger V, Rutenfranz J, Messel S (1974) Physical performance capacity of children in norway. European Journal of Applied Physiology and Occupational Physiology 33:265-274. https://doi.org/10.1007/BF00430234

Lind F, Hesser CM (1984) Breathing pattern and lung volumes during exercise. Acta Physiol Scand 120:123-129. https://doi.org/10.1111/j.1748-1716.1984.tb07381.x

MacLean JE, DeHaan K, Fuhr D, Hariharan S, Kamstra B, Hendson L, Adatia I, Majaesic C, Lovering AT, Thompson RB, Nicholas D, Thebaud B, Stickland MK (2016) Altered breathing mechanics and ventilatory response during exercise in children born extremely preterm. Thorax 71:1012-1019. https://doi.org/10.1136/thoraxjnl-2015-207736

Menache MG, Hofmann W, Ashgarian B, Miller FJ (2008) Airway geometry models of children's lungs for use in dosimetry modeling. Inhal Toxicol 20:101-126. https://doi.org/10.1080/08958370701821433

Miller FJ, Asgharian B, Schroeter JD, Price O (2016) Improvements and additions to the Multiple Path Particle Dosimetry model. J Aerosol Sci 99:14-26. https://doi.org/https://doi.org/10.1016/j.jaerosci.2016.01.018

O'Donnell DE, Maltais F, Porszasz J, Webb KA, Albers FC, Deng Q, Iqbal A, Paden HA, Casaburi R (2014) The continuum of physiological impairment during treadmill walking in patients with mild-to-moderate COPD: patient characterization phase of a randomized clinical trial. PLoS One 9:e96574. https://doi.org/10.1371/journal.pone.0096574

Ofir D, Laveneziana P, Webb KA, O'Donnell DE, Lam YM (2008) Mechanisms of Dyspnea during cycle exercise in symptomatic patients with GOLD stage I chronic obstructive pulmonary disease. Am. J. Respir. Crit. Care Med. 177:622-629. https://doi.org/10.1164/rccm.200707-1064OC

Prado DM, Braga AM, Rondon MU, Azevedo LF, Matos LD, Negrão CE, Trombetta IC (2010) Cardiorespiratory responses during progressive maximal exercise test in healthy children. Arq Bras Cardiol 94:493-499. https://doi.org/10.1590/s0066-782x2010005000007

Rowland TW, Cunningham LN (1997) Development of Ventilatory Responses to Exercise in Normal White Children: A Longitudinal Study. Chest 111:327-332. https://doi.org/https://doi.org/10.1378/chest.111.2.327

Sharratt MT, Henke KG, Aaron EA, Pegelow DF, Dempsey JA (1987) Exercise-induced changes in functional residual capacity. Respir Physiol 70:313-326. https://doi.org/10.1016/0034-5687(87)90013-2

U.S. EPA (2011). Exposure Factors Handbook: 2011 Edition (Final Report). Inhalation Rates., U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-09/052F

Yeh HC, Schum GM (1980) Models of human lung airways and their application to inhaled particle deposition. Bull Math Biol 42:461-480. https://doi.org/10.1007/BF02460796