

## Supplementary material to

Combination of toxicological and epidemiological approaches for estimating the health impact of atmospheric pollutants. A Proof of Concept for NO<sub>2</sub>.

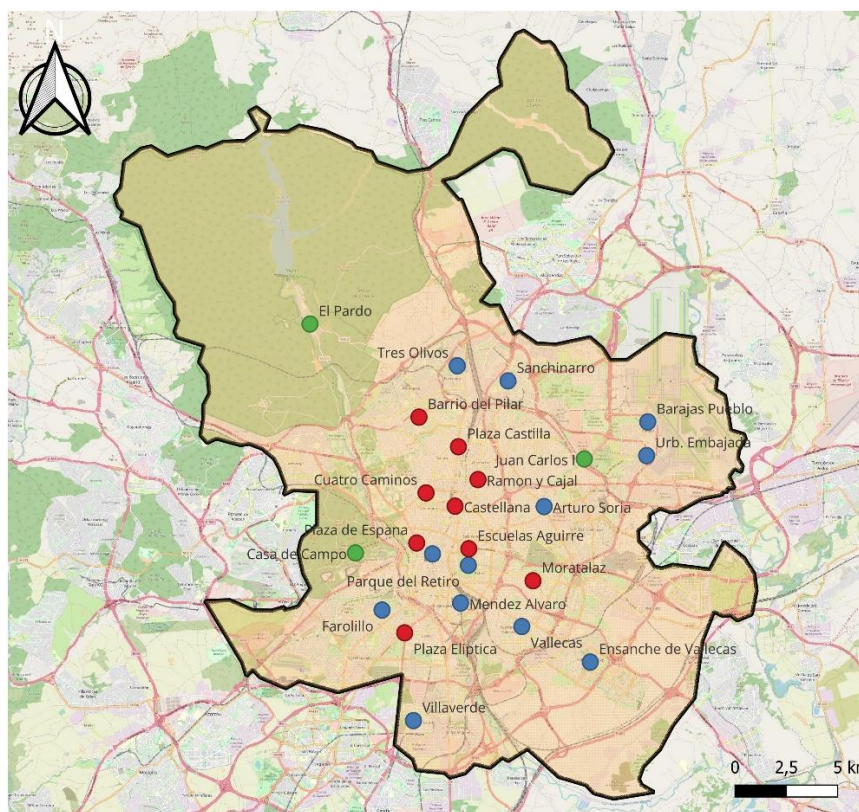
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Official air quality network of Madrid City council

Kind of monitoring station:

- Urban traffic
- Urban background
- Suburban
- Madrid municipality limit



MONITORING STATION	ADDRESS	LONGITUDE (ETRS89)	LATITUDE (ETRS89)	TPOLOGY
Plaza de España	Plaza de España	3°42'43.91"O	40°25'25.98"N	Urban traffic
Escuelas Aguirre	Entre C/ Alcalá y C/ O' Donell	3°40'56.22"O	40°25'17.63"N	Urban traffic
Ramón y Cajal	Avda. Ramón y Cajal esq. C/ Príncipe de Vergara	3°40'38.50"O	40°27'5.29"N	Urban traffic
Arturo Soria	C/ Arturo Soria esq. C/ Vizconde de los Asilos	3°38'21.17"O	40°26'24.20"N	Urban background
Villaverde	C/ Juan Peñalver	3°42'47.89"O	40°20'49.74"N	Urban background
Farolillo	C/ Farolillo - C/ Ervigio	3°43'54.61"O	40°23'41.22"N	Urban background
Casa de Campo	Casa de Campo (Terminal del Teleférico)	3°44'50.44"O	40°25'9.69"N	Suburban
Barajas Pueblo	C/ Júpiter, 21	3°34'48.10"O	40°28'36.93"N	Urban background
Plaza del Carmen	Plaza del Carmen esq. Tres Cruces	3°42'11.40"O	40°25'9.15"N	Urban background
Moratalaz	Avda. Moratalaz esq. Camino de los Vinateros	3°38'43.02"O	40°24'28.64"N	Urban traffic

<b>MONITORING STATION</b>	<b>ADDRESS</b>	<b>LONGITUDE (ETRS89)</b>	<b>LATITUDE (ETRS89)</b>	<b>TPOLOGY</b>
<b>Cuatro Caminos</b>	Avda. Pablo Iglesias esq. C/ Marqués de Lema	3°42'25.64"O	40°26'43.97"N	<b>Urban traffic</b>
<b>Barrio del Pilar</b>	Avda. Betanzos esq. C/ Monforte de Lemos	3°42'41.53"O	40°28'41.64"N	<b>Urban traffic</b>
<b>Vallecas</b>	C/ Arroyo del Olivar esq. C/ Río Grande.	3°39'5.50"O	40°23'17.33"N	<b>Urban background</b>
<b>Méndez Álvaro</b>	C/ Juan de Mariana / Plaza Amanecer Méndez Álvaro	3°41'12.57"O	40°23'53.17"N	<b>Urban background</b>
<b>Castellana</b>	C/ José Gutiérrez Abascal	3°41'25.34"O	40°26'23.61"N	<b>Urban traffic</b>
<b>Parque del Retiro</b>	Paseo Venezuela- Palacio de Velázquez	3° 40' 57"O	40° 24' 52"N	<b>Urban background</b>
<b>Plaza Castilla</b>	Plaza Castilla (Canal)	3°41'19.48"O	40°27'56.10"N	<b>Urban traffic</b>
<b>Ensanche de Vallecas</b>	Avda. La Gavia / Avda. Las Suertes	3°36'43.70"O	40°22'22.84"N	<b>Urban background</b>
<b>Urb. Embajada</b>	C/ Riaño (Barajas)	3°34'50.03"O	40°27'44.51"N	<b>Urban background</b>
<b>Plaza Elíptica</b>	Plaza Elíptica - Avda. Oporto	3°43'7.54"O	40°23'6.10"N	<b>Urban traffic</b>
<b>Sanchinarro</b>	C/ Princesa de Éboli esq. C/ María Tudor	3°39'37.86"O	40°29'39.12"N	<b>Urban background</b>
<b>El Pardo</b>	Avda. La Guardia	3°46'28.62"O	40°31'4.97"N	<b>Suburban</b>
<b>Juan Carlos I</b>	Parque Juan Carlos I (frente oficinas mantenimiento)	3° 36' 33"O	40° 27' 55"N	<b>Suburban</b>
<b>Tres Olivos</b>	Plaza Tres Olivos	3°41'23.03"O	40°30'1.97"N	<b>Urban background</b>

Figure S1. Location of the monitoring stations.

### **Example for estimation citizens' exposure and adversity from monitoring data**

Considering the spatial and temporal variability, and the mobility of citizens within the city, monitoring data collected from permanent monitoring stations can be used for estimating exposure and adversity levels for different population groups. As the results have confirmed a high temporal variability in daily averages within and among monitoring stations, the proposed approach for estimating adversity levels at different temporal patterns may offer relevant information. To exemplify the implementation of this approach, Figure S2 presents the expected variability in 1, 2 and 7 days adversity levels for three population groups, representing, low, average and high expected exposure levels. For simplification, we selected only two monitoring stations, representing high and low measured levels. The assumptions used for this example are as follows:

- Low exposure group: 90% of the day expended in low exposure areas, and 10% of the day expended in high exposure areas
- Average exposure group: 50% of the day expended in low exposure areas, and 50% of the day expended in high exposure areas
- High exposure group: 10% of the day expended in low exposure areas, and 90% of the day expended in high exposure areas

Due to the temporal variability, the exposure and adversity levels will not only depend on the percentages, but also on the actual days. A Monte Carlo simulation using Crystal Ball with 10000 replications was used for predicting the probability distributions associated to each group. Results are presented as the distribution of adversity percentiles for each population group.

The results presented in Figure S2 confirm the need for considering different population patterns for a proper assessment of subpopulation groups, as for the high exposure group, the estimated adversity levels for a significant number of days will be higher than that expected to the average group even accounting for the variability.

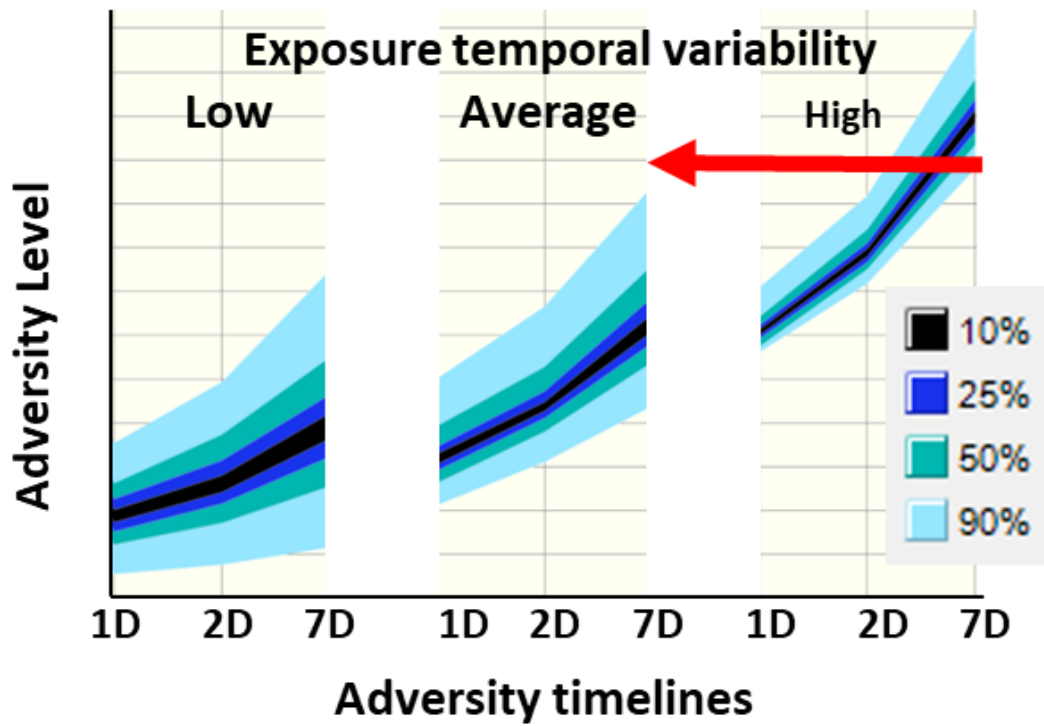


Figure S2. Distribution of adversity levels as percentiles of a Monte Carlo simulation for three generic groups representing low, average and high exposure levels.

**Table S1. Effects and adversity levels observed in toxicological animal studies after acute exposure to NO2. \*Adversity level score: (0-33): early interim effects; (34-99): General events; (100): Mortality**

Study	Spp	Concentration		Exposure				Adversity level*	Effects
		ppm	ug/m3	daily fraction	daily average	days	months	score	
Rombout et al., 1986 <sup>12</sup> Experiment 1	rat	10,46	20000	1	20000	1	0,033	40	Loss of cilia, necrosis of epithelial alveolar cells type I, slight increase of cells type II and of alveolar macrophages
	rat	10,46	20000	1	20000	2	0,066	45	As above and slight hypertrophy of bronchiolar epithelia, higher increase of type II cells, and slight increases of thickened centrolobular septa
	rat	10,46	20000	1	20000	4	0,13	55	As above, higher hypertrophy and slight hyperplasia of bronchiolar epithelium
	rat	10,46	20000	1	20000	8	0,26	60	Similar but enhanced effects in hyperplasia of bronchiolar epithelium
	rat	10,46	20000	1	20000	16	0,53	60	As above, no further progression, not recovery
	rat	10,46	20000	1	20000	28	1	60	As above, no further progression not recovery
	Rombout et al., 1986 <sup>12</sup> Experiment 2	rat	0,523	1000	1	1000	28	1	0
rat		1,307	2500	1	2500	28	1	0	No observed effects
rat		2,615	5000	1	5000	1	0,033	0	No observed effects
rat		2,615	5000	1	5000	2	0,066	40	Slight loss of cilia and slight hypertrophy bronchiolar epithelia, increase of alveolar macrophages and thickened centroacinar septa
rat		2,615	5000	1	5000	4	0,13	45	As above and increased loss of cilia and hypertrophy bronchiolar epithelia. Also hyperplasia bronchiolar epithelia.
rat		2,615	5000	1	5000	8	0,26	55	As above and sever hyperplasia of bronchiolar epithelium
rat		2,615	5000	1	5000	16	0,53	55	As above, no further progression not recovery

Study	Spp	Concentration		Exposure				Adversity level*	Effects
		ppm	ug/m3	daily fraction	daily average	days	months	score	
Rombout et al., 1986 <sup>12</sup>	rat	10,46	20000	0,25	5000	1	0,033	0	No observed effects
	rat	10,46	20000	0,25	5000	2	0,066	40	Loss of cilia, increase in alveolar wall thickness
Experiment 3	rat	10,46	20000	0,25	5000	4	0,13	45	Loss of cilia, slight thickening of centroacinar septa and focal hypertrophy of the bronchiolar epithelium
	rat	10,46	20000	0,25	5000	8	0,26	55	Similar but enhanced effects
	rat	10,46	20000	0,25	5000	16	0,53	55	As above, with hyperplasia in addition to hypertrophy
	rat	10,46	20000	0,25	5000	28	1	55	As above, no further progression not recovery
	rat	10,46	20000	1	20000	2	0,066	50	Loss of cilia, hypertrophy, increase of alveolar macrophages
	rat	10,46	20000	1	20000	4	0,13	55	Similar effects with higher severity and increase in alveolar wall thickness
	rat	10,46	20000	1	20000	8	0,26	55	As above, no further progression not recovery
	rat	10,46	20000	1	20000	16	0,53	60	As above and distended alveoli
	rat	10,46	20000	1	20000	28	1	70	As above and significant accumulation of macrophages