Spatial variations and development of land use regression models of oxidative potential in ten European study areas

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Abstract

Oxidative potential (OP) has been suggested as a health-relevant measure of air pollution. Little information is available about OP spatial variation and the possibility to model its spatial variability. Our aim was to measure the spatial variation of OP within and between 10 European study areas. The second aim was to develop land use regression (LUR) models to explain the measured spatial variation.

OP was determined with the dithiothreitol (DTT) assay in ten European study areas. DTT of PM2.5 was measured at 16-40 sites per study area, divided over street, urban and regional background sites. Three two-week samples were taken per site in a one-year period in three different seasons. We developed study-area specific LUR models and a LUR model for all study areas combined to explain the spatial variation of OP.

Significant contrasts between study areas in OP were found. OP DTT levels were highest in southern Europe. DTT levels at street sites were on average 1.10 times higher than at urban background locations.

In 5 of the 10 study areas LUR models could be developed with a median R^2 of 33%. A combined study area model explained 30% of the measured spatial variability. Overall, LUR models did not explain spatial variation well, possibly due to low levels of OP DTT and a lack of specific predictor variables.

Keywords: Oxidative potential, DTT, LUR, PM2.5, Spatial variation*

* Abbreviations: ESCAPE, European Study of Cohort for Air Pollution Effects; TRANSPHORM**,** Transport related Air Pollution and Health impacts - Integrated Methodologies for Assessing Particulate Matter; DTT **dithiothreitol** ROS reactive oxygen species, EC/OC, elemental/organic carbon; PAH, p**olycyclic aromatic hydrocarbons; B[a]P, benzo[a]pyrene**, GIS, Geographic Information Systems; LUR, Land Use Regression; NOx, nitrogen oxides; NO2, nitrogen dioxide; PM2.5, mass concentration of particles less than 2.5 mm in size; PM2.5 absorbance, measurement of the blackness of PM2.5 filters, this is a proxy for elemental carbon, which is the dominant light absorbing substance; PM10, mass concentration of particles less than 10 mm in size; RB, regional background; S, Street; EPA, United States Environmental Protection Agency; LUR, Land Use Regression; RMSE, Root Mean Squared Error.

1. Introduction

Exposure to air pollution has been associated with morbidity and mortality (Brunekreef, Holgate 2002, Pope, Dockery 2006) Epidemiological studies have used mostly the mass of particle matter (PM) with diameters smaller than 10 or 2.5 µm (PM10, PM2.5, respectively) for assessment of exposure to air pollution. The composition and size distribution of PM differs substantially in space and time. There is increasing evidence that the magnitude of adverse health effects depends on PM chemical composition and size distribution (Stanek et al. 2011, Kelly, Fussell 2012). Oxidative potential (OP) has been suggested as a health relevant parameter for epidemiological studies (Borm et al. 2007).

Oxidative potential is defined as a measure of the capacity of PM to oxidize target molecules. Because OP integrates various PM characteristics (e.g. size, chemical composition, biological properties, surface) it might be a more health relevant PM metric than PM mass or single PM compounds (Boogaard et al. 2012, Borm et al. 2007). However, few epidemiological studies have evaluated whether OP of PM predicts health effects better than PM mass. Little is known about the spatial variation of oxidative potential, which is needed to assess whether OP of PM predicts health effects related to long-term exposure better than PM2.5 or constituents of PM2.5. Previous studies have documented variability of OP measured with various assays within metropolitan areas (US studies) (Vedal et al. 2013, Hu et al. 2008, Landreman et al. 2008) or single countries (Yang et al. 2014, Yang et al. 2015, Boogaard et al. 2012). Only one study has evaluated spatial contrast between European cities, based upon 20 urban background sites (Kunzli et al. 2006). The authors found significant spatial contrast in the OP levels measured as the ability of PM to generate ·OH in the presence of hydrogen peroxide.

Several chemical assays exist to assess the oxidative potential of PM. They differ from each other in sensitivity to the reactive oxygen species (ROS) generating compounds and analytical method (Ayres et al. 2008). One commonly used assay is based on the consumption of dithiothreitol (DTT) related to the ability of redox active compounds to transfer electrons from DTT to oxygen (Cho et al. 2005, Kumagai et al. 2002). The DTT assay is especially sensitive to organic components such as quinones.

Land use regression models (LUR) have been used increasingly to model the spatial variation of the long term average concentration of the PM2.5, PM10 and the traffic-related pollutants NO_2 and Black carbon (Beelen et al. 2013, Eeftens et al. 2012, Hoek et al. 2008). To our knowledge only two studies reported LUR models for oxidative potential (Yanosky et al. 2012, Yang et al. 2015). Yanosky et al. (2012) modeled OP of PM10 in London, where OP was measured as the depletion rate of antioxidant reduced glutathione (OP^{GSH}) (Yanosky et al. 2012). Yang et al (2015) recently presented LUR models for 40 Dutch sites for two different OP metrics: DTT and ESR (electron spin resonance).

The first aim of this study was to determine the spatial contrast of oxidative potential within and between 10 European study areas. The second aim was the development and evaluation of LUR models of oxidative potential.

In ten European study areas we measured oxidative potential with the DTT assay. The study areas were part of two European projects: ESCAPE (European Study of Cohort for Air Pollution Effects) and TRANSPHORM (Transport related Air Pollution and Health impacts - Integrated Methodologies for Assessing Particulate Matter) (Cyrys et al. 2012, Tsai et al. 2015, Eeftens et al. 2012).. In the

framework of these projects concentrations of the pollutants NOx, NO_2, PM2.5, PM10, PM2.5 absorbance and elemental composition were measured in 20 study areas. Measured concentrations and LUR models for these pollutants have been published (Beelen et al. 2013, Eeftens et al. 2012, Cyrys et al. 2012, de Hoogh et al. 2013, Tsai et al. 2015). In 10 study areas additional characterization of PM was performed, including elemental and organic carbon (EC, OC) and polycyclic aromatic hydrocarbons (PAH) (Jedynska et al. 2014b), levoglucosan (Jedynska et al. 2015) and oxidative potential.

2. Methods

2.1 Sampling campaign

The ESCAPE sampling campaign has been described in detail previously (Cyrys et al. 2012, Eeftens et al. 2012). In 10 of the ESCAPE study areas (Table 1, Figure 1), oxidative potential was determined with the DTT assay. All study areas included regional and urban background and major street sites. A street site was considered a site in a major road carrying at least 10,000 vehicles per day. An urban background site was defined as a site with fewer than 3000 vehicles per day passing within a 50 m radius. Regional sites were located in small villages typically near a major city, though the distinction between regional and urban background was not strictly defined

Three 14-day integrated samples were collected for each site in a one year period. In four study areas sampling was conducted in 2009, in the other six in 2010. Samples were collected during three seasons: winter, summer and intermediate season (spring or autumn). Due to lack of sampling equipment in Munich/Augsburg, no samples were taken from December to February. Sampling of PM2.5 was performed with the Harvard impactor (Eeftens et al. 2012).. For the OP analysis a quartz filter (QMA,Whatman) was used. We used quartz filters for oxidative potential measurements as these were the only filters available for us to use for OP determination. In a recent comparison study, OP DTT levels on quartz filters were about 20% lower than on Teflon filters. Temporal correlation between DTT on both filter types was high (R=0.81) (Yang et al. 2014). The partners in all study areas used identical sampling protocols and criteria for the selection of sampling sites (Eeftens et al. 2012).

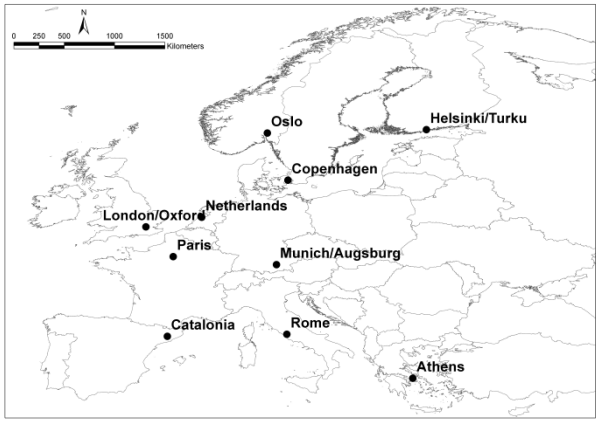

Figure 1. Ten European study areas where oxidative potential by DTT assay was measured

Table 1. Description of study areas. RB –regional background, UB – urban background, S – street location

Country	Study area	Sampling period	Sites	Site types		
				RB	UB	S
Norway	Oslo	05.02.2009 – 29.01.2010	19	2	9	8
Finland	Helsinki/Turku	27.01.2010 – 26.01.2011	20	2	10	8
Denmark	Copenhagen	19.11.2009 – 17.11.2010	20	3	6	11
United Kingdom	London/Oxford	26.01.2010 – 18.01.2011	20	1	12	7
The Netherlands	Rotterdam, Amsterdam, Groningen, Amersfoort	17.02.2009 – 19.02.2010	16	4	4	8
Germany	Munich/Augsburg	01.03.2009 – 05.11.2009	20	5	6	9
France	Paris	04.01.2010 – 04.01.2011	20	4	9	7
Italy	Rome	27.01.2010 – 26.01.2011	20	2	8	10
Spain	Catalonia (Barcelona, Girona, Sabadell)	14.01.2009 – 14.01.2010	40	4	13	23
Greece	Athens	21.04.2010 – 27.04.2011	20	1	12	7

2.2. Analytical methods

2.2.1 Filter extraction for oxidative potential measurements

All OP measurements took place in one laboratory (TNO). 2.4 cm^2 of each quartz filter (30% of the filter) was extracted in 20 ml ethanol for 1 hour in an ultrasonic bath. Further, the extracts were filtered with 0.45 µm PTFE syringe filters to remove quartz particles and the insoluble PM fraction and dried under constant flow of nitrogen. At the end extracts were reconstituted in 100 µl ethanol and 900 µl MiliQ water. The extraction method applied in this study included only the ethanol soluble PM fraction contributing to OP level measured with DTT assay.

2.2.2 DTT assay

The DTT assay measures the presence of reactive oxygen species via formation of DTT-disulfide due to transfer of electrons from DTT to ROS by recycling chemicals such as quinones (Cho et al. 2005). The DTT assay measures the presence of reactive oxygen species via formation of DTT-disulfide due to transfer of electrons from DTT to ROS by recycling chemicals such as quinones (Cho et al., 2005) and elements (Charrier et al., 2012; Charrier, et al. ACP 2015). Several of the most recent literature studies report about evidence for the importance of soluble transition metals being reactive in the DTT assay. Although the net effect of elements in the DTT assay is not yet completely clear (Sauvain, 2013, Perrone, et al., 2016).

Aliquots of samples extracts were incubated at 37 ºC with DTT(100 mM) (Sigma, Zwijndrecht) in potassium phosphate buffer at pH 7.4 The reaction was stopped at designated time points (0, 10, 20, 30, 40 and 50 min), adding 10% trichloroacetic acid.

Finally, 0.5 mL of 0.4M Tris–HCl, pH 8.9 containing 20mM EDTA and 30 mL of 10mM DTNB5, 50-Dithiobis(2-nitrobenzoic acid) (DTNB) (Sigma) were added.The concentration of the formed 5-mercapto-2-nitrobenzoic acid was measured by its absorption at 412 nmand the rates are calculated using linear regression of absorbance against time. The results are expressed as nmol DTT/min*m^3 .

A soot sample obtained from exhaust pipe of city busses was used as a positive control and ultrapure water as a negative control. The blanks and control sample were treated the same way as all other samples

2.2.3 Quality control

To maximize comparability of the sampling in different countries, sampling and measurement procedures were conducted according to standard protocols. All OP analyses were performed centrally in the TNO lab in the Netherlands. We did not have enough equipment available to include field blanks and duplicates for OP analyses. OP methods used at TNO have been validated according to the Dutch national norm (NEN-7777, 2003 https://www.nen.nl/NEN-Shop/Norm/NEN-7777C12012-en.htm). The following checks were performed in the laboratory: Mili-Q blanks, quality control samples – soot sample as a positive control for OP DTT assay.

2.2.4 EC/OC, PAH, hopanes, steranes, levoglucosan, PM2.5, NOx and elemental composition

The analytical methods of EC/OC, PAH, hopanes/steranes, levoglucosan, PM2.5, NO2 and elemental composition were published previously (Jedynska et al. 2014b) and are summarized in the Online supplement.

2.3 Adjustment for temporal variability

The three 14-day average - samples were used to calculate the annual average level of oxidative potential. Due to lack of equipment we could not collect samples simultaneously at all sites, and as a result the simple average from the concentrations in the three sampling periods could reflect both spatial and temporal variation. In order to correct for temporal variation, a (background) reference site was continuously measured in each study area during the sampling period. Our correction procedure followed the modified ESCAPE procedure used for EC/ OC, PAH, hopanes/steranes and levoglucosan (Eeftens et al. 2012, Cyrys et al. 2012, Jedynska et al. 2014b). Briefly, we evaluated which of the pollutants measured at the reference site, correlated best with OP. The temporal correlation was calculated for each site between OP and the main ESCAPE pollutants NO_x, NO_2, PM2.5, PM2.5 absorbance and PM10 based upon three samples. The median correlation per study area was calculated and the pollutant with the highest median correlation with OP was used for correction of temporal variation, using the ratio method as we did for EC/OC, PAH, hopanes/steranes and levoglucosan (Jedynska et al. 2014b).

2.4 Predictor data for LUR model development

Derivation of predictor variables has been presented in detail (Eeftens et al. 2012, Beelen et al. 2013). Briefly, the predictor variables mainly describe potential emission sources such as traffic, industry or residential emissions related. The predictor variables were determined for each sampling site using a geographical information system (GIS). First, the coordinates of each sampling site were determined using repeated Global Positioning System (GPS) measurements, supplemented by careful checking of the site location using the most detailed local map in a GIS. Second, GIS analyses were conducted to derive the values for the predictor variables for the coordinates of the monitoring sites. GIS analyses included distance from the sampling site to sources such as major roads and the amount of (proxies of) potential sources in a circle with a predefined radius (called a buffer) around the sampling site. Examples include the product of traffic intensity and road length in a buffer of 50m

and population density in a buffer of 1000m. More detailed explanation of GIS analyses and their use in LUR modelling can be found in previous reviews (Jerrett et al. 2005). The buffer sizes were selected to take account of known dispersion patterns. Both small-scale and larger-scale buffer sizes were used for the traffic variables indicating two scales of influence: near source and urban background levels representing larger-area traffic density (Beelen et al. 2012). A detailed description of the variables is presented in online supplement Table S1.

2.5 LUR model development

We first prepared maps of the measured OP for each of the 10 study areas to evaluate spatial patterns. using ArcGIS version 10.2.1. We calculated the Moran's I statistic that tests for presence of spatial autocorrelation. Moran's I ranges from -1 to +1 with -1 / (N-1) indicating no spatial autocorrelation (N=number of observations). Moran's I was calculated with the Variogram procedure of the Statistical Analysis System version 9.4.

LUR models were developed by the first author using the ESCAPE method (Beelen et al. 2013, Eeftens et al. 2012, de Hoogh et al. 2013). Briefly, adjusted annual average concentration of oxidative potential and predictor variables were used for LUR development. A supervised stepwise method was used to obtain the linear regression model with the highest explained variance (R^2). At every step the variable with the highest R^2 was added to the model if it improved model's adjusted R^2 by at least 1% and had the same effect direction as decided a priori e.g. higher traffic intensity predicts higher OP. The final model was evaluated for statistical significance (variables removed when p-value >0.10), collinearity (variables with Variance Inflation Factor (VIF) > 3 were removed) and influential observations (models with Cook's D > 1 were further examined). The final models were evaluated by leave-one-out cross validation (LOOCV)

Models were developed for each of the 10 study areas separately and for the combined dataset. Wang et al (2014) recently documented the feasibility of developing European models combining all ESCAPE study areas for PM2.5, PM2.5 absorbance and NO_2 (Wang, Beelen et al. 2014). We developed combined study area models with indicators for study area and another model with the measured regional OP background in each study area as a predictor variable. The latter approach is comparable to the multi-city model for PM2.5, PM2.5 absorbance and NO_2 (Wang, Beelen et al. 2014). A limitation of developing a combined area model was that measurements were conducted in 2009 or 2010 in the various areas. Routine measurements of PM2.5 and PM10 concentrations obtained from Airbase did not differ between 2009 and 2010 (Eeftens et al, 2012). Based on those findings we expect no significant difference in OP DTT concentrations between 2009 and 2010.

2.6 Data analysis

All measurements' results were analyzed centrally at TNO. Statistical analyses were performed with the SPSS statistical program (IBM SPSS Statistics 20).

We assessed the significance of differences of adjusted annual OP averages between study areas with analysis of variance (ANOVA). Student's t-tests were used to evaluate the difference between site types and between seasons. We analyzed seasonal differences based on all individual measurements divided into the warm (April – September) and cold period (October – March).

3. Results and discussion

The detection limit (LOD) of DTT, calculated as three times the standard deviation of laboratory blanks, was 0.078 nmolDTT/min*m^3. 15% of all samples gave results below the LOD. The uncertainty of the DTT assay is 24%. Calculation of uncertainty (Uc) was based on: reproducibility (vc), recovery (utv) and accuracy of the calibration standard (uj) according to the following formula:

$$Uc = \sqrt{(vc)^2 + (uj)^2 + (utv)^2}$$

Shewhart chart was used to monitor the quality of the results of the control sample (soot) which was measured every measurement day. 82% of the results where within ±2*STD from the average result obtained after the first OP DTT 10 measurements. Taken all measurements of the control samples the relative standard deviation was 22%. The repeatability of Mili-Q blanks was 16%.

Temporal adjustment

The main focus is on adjusted annual average concentrations. In five study areas OP DTT was corrected for temporal variation with PM2.5, in four with NO_x and in one with PM2.5 absorbance. The high correlation (R>0.90 in all areas except Helsinki, where R was 0.60) between the selected pollutant and OP at the sampling sites documents that the temporal variation of OP was well reflected by these pollutants. Adjusted and unadjusted annual OP averages were mostly highly correlated (Table S2). Pearson correlation coefficients were between 0.65 and 0.98 (Table S2). This documents that the adjustment did not change the results much.

3.1 Within and between study area contrast

The spatial variation within and between study areas is presented in Figure 2 and Table 2. Maps of OP for each of the 10 study areas are shown in supplement figure S2. Levels of OP DTT across Europe differed significantly (Figure 2, Table 2). The lowest OP DTT level were found in London (0.14 nmolDTT/min * m^3) and two Nordic areas – Oslo and Helsinki/Turku (0.13 and 0.15 nmolDTT/min * m^3, respectively).
OP DTT levels were highest in southern study areas, but the differences between the three southern and the three northern study areas were smaller (south/north ratio = 1.5) than we found for traffic-related pollutants including NO_2 and EC (south/north ratio – 2.2) and for PM2.5 mass (south/north ratio – 2.1), (Eeftens et al. 2012, Cyrys et al. 2012, Jedynska et al. 2014b).

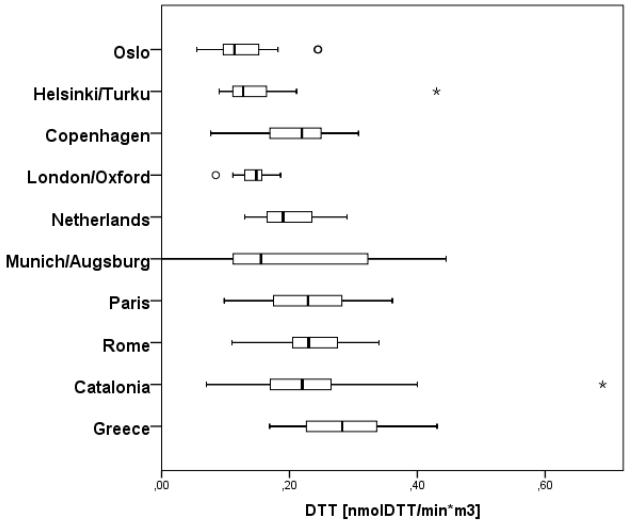

Figure 2. Distribution of OP DTT (nmolDTT/min * m^3) in different study areas. Median, 25th and 75th percentiles are shown in the box, whiskers indicate 10th and 90th percentiles and individual outliers are shown.

Table 2. Mean and range of annual average oxidative potential for 10 European study areas

Study area		DTT (nmolDTT/min * m^3)			
	N	Mean[1]	Min	Max	Range/Mean [%]
Oslo	19	0.13	0.06	0.25	149
Helsinki/Turku	20	0.15	0.09	0.43	229
Copenhagen	20	0.21	0.08	0.31	109
London/Oxford	20	0.14	0.08	0.19	71
Netherlands	16	0.20	0.13	0.29	80
Munich/Augsburg	20	0.20	0.00	0.45	221
Paris	20	0.23	0.10	0.36	115
Catalonia	40	0.23	0.07	0.69	271
Rome	20	0.23	0.11	0.34	98
Athens	20	0.28	0.17	0.43	92

[1]Differences between study areas statistically significant (ANOVA, $p < 0.0001$)

Table 3. Difference of annual average oxidative potential levels between site types (ratios RB/UB and S/UB)

	DTT (nmolDTT/min * m^3)	
	RB/UB	S/UB
Oslo	0.82	0.88
Helsinki/Turku	0.85	0.71
Copenhagen	1.22	1.05
London/Oxford	1.12	1.06
Netherlands	0.90	1.14
Munich/Augsburg	1.73	1.11
Paris	0.95	1.15
Rome	1.63	1.12
Catalonia	0.99	1.10
Athens	0.63	1.21
Median	0.97	1.10

The smaller contrast across Europe is consistent with the small difference between street and urban background locations found in this study (Table 3). In 8 of the 10 study areas, concentrations at the street sites were slightly higher than at the urban background sites with a median S/UB ratio of 1.10. Our findings are in line with a few previous studies which also reported low contrast of OP DTT between street and background sites. In a recent study based upon extraction of the Teflon PM2.5 filters of all 40 ESCAPE sites in the Netherlands/Belgium, the street locations had 1.2 times higher OP DTT than urban background sites (Yang et al. 2015). In our study, the Dutch S/UB ratio, based on 16 of these 40 sites, was very similar – 1.14.

In another Dutch study with five sites, OP DTT was 1.2 times higher at a busy urban street site than at urban background (Janssen et al. 2014). The ratio between a highway site to an urban background

site was higher (ratio 2.1). In our study we did not have street sites with as heavy traffic as on highways.
In a study investigating OP in the Los Angeles harbor area, a modest contrast in DTT results between different sites was found (Hu et al. 2008). The ratio between traffic and background sites was on average 1.3.
Our study conducted in 10 different European study areas supports a growing literature that OP DTT does not reflect large urban traffic contrasts (Yang et al. 2015, Janssen et al. 2014, Hu et al. 2008). The assay may respond to components from non-traffic sources resulting in a high background.

The OP DTT S/UB ratio found in our study was lower than for other pollutants measured at the same sites including NO_2, EC, PAH and OC (Eeftens, Tsai et al. 2012, Cyrys, Eeftens et al. 2012, Jedynska, Hoek et al. 2014b). As the DTT assay responds primarily to organic compounds, particularly the substantially lower contrast compared to OC (median S/UB = 1.32) and PAH (median S/UB = 1.44) is remarkable. We did not measure quinones, components which are thought to especially affect the DTT assay.
Quinones are oxygenated aromatic compounds e.g. oxy-PAH, emitted during incomplete combustion processes including traffic (Jedynska et al. 2015) and formed during photochemical transformation of emitted parent-PAHs by atmospheric oxidants (Alam et al. 2013).
There was no consistent difference between urban and regional background sites (median RB/UB = 0.97). In four study areas (London/Oxford, Munich/Augsburg, Copenhagen, Rome), OP DTT was higher at the regional sites. In three of these areas (London, Munich/Augsburg, Rome) OC concentrations were also increased at the regional sites (Jedynska et al. 2014b). This suggests that sources of organic components that affect OP DTT may be present in more rural areas. At the regional background sites, Yang et al found lower OP DTT level than at the urban background sites (ratio 0.8), consistent with our results for the Netherlands (0.9).

The mean OP DTT levels were only 2-4 times higher than the LOD (Table 2). OP DTT levels were also low compared to levels found in other studies (Saffari et al. 2014, Janssen et al. 2014, Yang et al. 2014). The low OP DTT concentrations were related to the use of quartz filters (Yang et al. 2014). We furthermore only extracted a section of the filter, as we also determined EC/OC and levoglucosan on the same filter. Quartz filters for PM collection in order to determine oxidative potential are not very common. In most studies PM was collected in a solution with the Versatile Aerosol Concentrator Enrichment System (VACES) (Cho et al. 2005, Ntziachristos et al. 2007) or Teflon filters were used (Janssen et al. 2014, Kunzli et al. 2006). We found one study where quartz filters were used for OP DTT measurements (Vedal et al. 2013). Yang et al. reported significantly lower OP levels for samples taken on quartz filters than on Teflon filters for four different OP assays, including DTT, with 20% lower results than samples taken on Teflon filters (Yang et al. 2014). The reported differences were presumably caused by lower extraction efficiency of samples taken on quartz filters or necessary filtration of the quarts extracts because of high concentration of quartz fiber in the extracts. The correlation between measurements on quartz and Teflon was high (R=0.8). The correlation was based on 15 measurements taken at two sites. For the Dutch data, a direct comparison with OP DTT measured on ESCAPE Teflon filters was available from another study (Yang et al. 2015). The correlation for the 16 sites was moderate for the unadjusted average concentration (R^2=0.26) and low for adjusted average concentration (R^2=0.12) (Figure S1).
Compared to the previous comparison study (Yang et al. 2014), the differences in absolute levels between Quartz and Teflon OP DTT were much larger. OP DTT levels on quartz in the previous comparison where 20% lower and highly correlated (R^2=0.66) with Teflon OP DTT (Yang et al,

2014). In the previous comparison all samples were analyzed in one laboratory, whereas in the current comparison samples were analyzed in different labs. The comparison of DTT analyses between the two laboratories revealed substantial differences in DTT levels with much lower TNO results, (Figure S2) (TNO REPORTI TNO-060-UTP-2013-00038). OP assays have not yet been standardized sufficiently to allow comparison of the results obtained at different laboratories. Absolute OP DTT values should therefore be interpreted with caution.

Overall, OP DTT was weakly correlated with other measured pollutants within areas (Table S3.). The highest median correlation was observed with OC and PAH.

3.2 Land use regression modelling

Individual study areas

For five out of ten study areas a LUR model could be developed (Table 4). The median R^2 for the 5 models was 33%. The lowest R^2 was found in Catalonia (R^2 = 13%) and the highest in The Netherlands and Oslo (73% and 66% respectively). In those two study areas the LOOCV R^2 was higher than 50%. No traffic related variables were included in the models. In three study areas variables describing population density were included. In two study areas variables related to green space were included. In four models only one significant predictor variable was identified. In Paris only altitude was included in the model.

Maps of OP for each of the 10 study areas are shown in supplement figure S4. Table S4 provides the Moran's I values testing for spatial autocorrelation and associated significance. Most of the maps and the Moran's I statistic document there is no spatial autocorrelation. In Catalonia, modest autocorrelation of borderline significance was present, mostly explained by somewhat higher OP values in the inner city of Barcelona. Consistently the LUR model included address density in a 500 m buffer. In Paris the map suggests some clustering of the highest values in the northeast part of the area (not statistically significant), likely leading to a model containing altitude as the sole predictor. The maps therefore do not clearly indicate presence of major sources contributing to OP that we missed in our GIS predictor data.

DTT model predictions were moderately correlated with both PM2.5 model prediction (median R=0.33) and with PM2.5 absorbance (median R=0.36) (Table 4).

In four of the five areas where no model was possible, the regional background OP measurements were higher than the urban background (Table 3). Our procedures did not allow a negative slope for address or population density, predictors with lower values at regional background sites. When an indicator variable for urban (0/1) was included and a negative slope allowed, models could be developed for Rome, Munich/Augsburg, London/Oxford and Helsinki/Turku with model R^2 of 17 to 52%. The rationale for this sensitivity analysis is that we are less certain about source impacts on OP DTT than on pollutants such as NO_2 and PM2.5 for which the procedures were developed. The Rome model included the indicator variable urban and distance to a major road (R^2=52%). The Munich/Augsburg model included the urban indicator variable and traffic load in a 100m buffer (R^2=30%). The London model included the urban indicator variable and major road length in a 100m buffer (R^2=17%). In Helsinki/Turku, a model was only possible including residential density in a 50m buffer if a high Cooks D was allowed (R^2=17%).

Combined study area model

A combined area model combining all ten study areas resulted in a model R^2 of 30%, with port and small scale residential density in addition to indicator variables for study areas (Table 4). A model with indicator variables alone explained 25% of the variability. We added study area indicators to avoid systematic differences between the countries (in e.g. GIS predictor data or climate) to affect the model, as we were mainly interested in intra-area variation. When we used measured regional background to characterize the study area, instead of indicator variables, a model was developed with four predictor variables that explained 24% of the variability in OP DTT. The developed model was: 0.0889+6.09E-09*PORT_5000+6.44E-11*Traffic load_1000+0.379*Regional Background+1.34E-6*Population_500, where PORT_5000 is harbour within 5000m, traffic load_1000 represents number of vehicles per day within 1000m from a sampling site times road length and Population_500 reflects number of inhabitants in a radius of 500m from a sampling site. In this model more of the variability was explained by GIS predictors representing specific sources (shipping and road traffic) while regional background OP DTT alone explained 5.3% of variability.

Overall, land use regression models did not explain spatial variation of OP DTT well. LUR models could be developed only for five out of ten study areas. The explained variance of the developed OP LUR models was low (median R^2 = 33%) in comparison to frequently modeled pollutants like PM2.5 or pollutants used as traffic markers – NO_2 or PM2.5 absorbance for which model R^2 higher than 70% were found in ESCAPE (Beelen et al. 2013, Eeftens et al. 2012). The model combining all ten study areas resulted in a low model R^2 as well, but the gap between model and leave-one out cross validation R^2 was much smaller than for the individual area models. The smaller gap is due to the larger number of monitoring sites to train the model (Wang et al., 2012). The combined area model contained more predictor variables (port, population density) than the study-area specific models (e.g. altitude and large scale natural land in Paris and Athens). Recently, several European and American studies reported large-scale LUR models for PM, NO_2 and soot (Novotny et al. 2011, Wang et al. 2014, Vienneau et al. 2013). Large-scale LUR models can provide improved prediction of pollutant concentrations for study areas with poor or no local models. Because of the non-contiguous study areas (Figure 1), application of the combined model in study areas not part of current monitoring is likely less reliable.

We found only two published study reporting a LUR for oxidative potential (Yanosky et al. 2012, Yang et al. 2015). In London, models were based on weekly averages of OP of PM10 measured with antioxidant reduced glutathione (GSH) at 66 sites. The explained variance of the developed model was 50%. The variables used were: PM10 brake and tire wear, emissions from all vehicles within 50m and NOx tailpipe emissions from heavy-goods vehicles within 100m. In our study we could not develop a LUR DTT model for London/Oxford study area, related to a different assay, the very low within study area contrast or a smaller number of locations than in the Yanosky study.

A recent Dutch study reported LUR models for two OP assays: DTT and ESR developed for the 40 Dutch ESCAPE sites. Reported R^2 of OP DTT LUR model was lower (60%) than the R^2 in our study for the Netherlands (73%). Both models differed in included variables. Our models included population density variable and variables describing natural areas while Yang et al developed a model containing regional OP DTT level, traffic related variables and natural area variable. The differences between two Dutch models might be caused by different number of used sites used for model development, different OP DTT levels (discussed before), and included regional OP DTT levels in the model.

Table 4. Description of LUR models for OP DTT (nmolDTT/min * m^3)

Study area	LUR model	n	R^2 [%]	LOOCV R^2 [%]	RMSE	R with PM2.5*	R with PM25abs*
Oslo	0.0547 + 0.000181 x HHOLD_300	19	66	59	0.0314	0.27*	0.14
Helsinki/Turku	NM						
Copenhagen	NM						
London/Oxford	NM						
Netherlands	0.193 + 0.0000149 x POP_300 - 0.00000104 x UGNL_300 - 2.376 x 10^{-9} x NATURAL_5000	16	73	50	0.0278	0.26*	0.25*
Munich/Augsburg	NM						
Paris	0.367 - 0.0164 x SQRALT	20	25	5	0.0633	0.33**	0.38**
Rome	NM						
Catalonia	1.268 + 0.00000641 x HDRES_500	39	12	6	0.070	0.30**	0.36**
Athens	0.324 - 5.045 x 10^{-9} x NATURAL_5000	20	33	22	0.064	0.49**	0.29*
Median			33	22			
Combined 10 area model with indicators for area	0.188 -0.10001 x area1 - 0.06504 x area2 -0.03328 x area3 - 0.08856 x area4 - 0.05127 x area5 + 0.00893 x area6 - 0.02609 area7 + 0.05424 x area8 + 0.00384 area9 + 6.82E-04 x PORT_5000 + 0.00000139 x HDLDRES_100	215	30	26	0.07677		

Description of variables used in the models: NATURAL Semi-natural and forested areas, UGNL Combined urban green and natural land, HDRES High density residential land, SQRALT Squared altitude, HHOLD number of households, POP number of inhabitants. HDLDRES Sum of High and Low density residential land.
NM = no model possible. R with PM2.5 is the correlation of the OP model prediction with the predictions of previously published PM2.5 models at sites not used for modelling. NM – no model possible. * Correlation between LUR model predictions of OP DTT and PM2.5 and PM2.5abs.significant at the 0.05 level, **. The correlation significant at the 0.01 level Study area indicators coded as 1 if site in specific area or 0 if not. Compared to Catalonia as the reference (n=40 sites).Area1 – Oslo, area2 – Helsinki/Turku, area3 – Copenhagen, area4 – London/Oxford, area5 – Netherlands, area6 – Munich/Augsburg, area7 – Paris, area8 – Rome, area9- Athens,

Performance of OP DTT models

The relatively poor general performance of LUR models for OP DTT is likely due to a combination of: 1. The low measured levels of OP DTT relative to the LOD; 2. The lack of specific GIS predictor variables for OP DTT; 3. Insufficient understanding of sources related to urban – rural differences of OP; 4. Data quality of GIS predictors..

First, due to the use of quartz filters, measured OP values did not exceed the LOD much and therefore the measurement error may have been relatively large. This is supported by the low to moderate correlation between our OP DTT measurements and OP DTT measurements on Teflon filters previously reported for the Dutch sites. Random error in a dependent variable in linear regression analysis does not lead to bias of the regression slopes of the model, but does lead to a loss in precision (Armstrong 1998).This implies that the correct LUR model may be identified but with low model R^2. This theory may apply more for the combined model based upon a large number of sites than for individual area models. Similar observations of a robust spatial model with a low model R^2 have recently been made in a LUR study based upon short-term monitoring (Montagne, Hoek et al. 2015). Short-term monitoring also resulted in large random error of concentration measurements per site.

Second, relatively low explained variance of LUR models for DTT might further be caused by the lack of variables describing oxidative potential sources other than traffic e.g. wood burning, specific industries or agricultural activities. Recently published land use regression models developed for components with other sources than traffic also had substantially lower explained variance than components with traffic markers (de Hoogh et al. 2013, Jedynska et al. 2015). LUR models for elemental composition of PM2.5 and PM10 were reported (de Hoogh et al. 2013). For elements representing traffic sources (Cu, Fe, Zn) models with high explained variances were found. Models for elements primarily related to non-traffic sources had more moderate explained variance (50-60%), still substantially higher than found in this study for OP. A moderate explained variance was also reported for the wood smoke marker levoglucosan in a subset of four of our study areas (Oslo, Netherlands, Munich, Catalonia)

(Jedynska et al. 2015). Recently, we also found moderate explained variance for LUR models for PAH and OC (median R^2 = 59% and 65%, respectively), probably due to the contribution of less well characterized sources of those pollutants (Jedynska et al. 2014a). Maps of OP DTT did not show significant spatial autocorrelation, suggesting we did not miss major local OP DTT sources.

Third, the observation that models could not be developed with our procedures especially in areas with higher regional background than urban background, suggests that we may not fully understand sources contributing to measured OP DTT. The rationale for specifying a fixed direction of slope for predictor variables is to avoid implausible models (Wang, 2012). OP may be affected more by secondary than primary pollutants, a hypothesis supported by the very small difference between measured OP at traffic and background locations and the absence of differences between urban and regional background sites. For example, reaction products of atmospheric oxidation reactions of PAH may have higher OP than the original PAH. Several PAH are semi-volatile, resulting in changes in the mixture with distance from the source. LUR models cannot easily accommodate atmospheric formation processes other than by using indicators for wind-dependent distance to large sources areas or indicator variables for region of the country. **Fourth**, low data quality of the GIS predictors may be an additional reason for the limited success of modelling OP. We have no solid information on validity of the predictor data in the ten study areas. Because we were able to develop LUR models with good performance for other pollutants including NO2, PM2.5 and the elemental and organic content of PM using the same predictor variables, it seems unlikely that data quality has been a major factor. This is supported by the lack of a clear geographical pattern in the ability to develop models and their performance.

3.3 Seasonal differences

Comparison of all measurements in two periods (cold and warm) showed higher concentrations during the cold period in 9 out of 10 study areas (Table S5). Helsinki/Turku had slightly higher concentrations in the warm period. The median cold/warm ratio was 1.51. The higher concentrations of

air pollutants in the cold period are mainly caused by higher pollutant emissions (heating) and poorer dispersion because of less vertical mixing during the cold period.
The OP DTT cold to warm ratio of 1.51 was lower than the ratio found for levoglucosan (6.3), a marker of wood combustion, with known high seasonality and ΣPAH (4.5), which are also influenced by more intensive domestic heating during winter (Jedynska et al. 2014b). The OP DTT cold to warm ratio was similar as the ratio for OC, which has various primary and secondary sources (1.9), and EC, used as traffic marker (1.3).
For air pollutants with traffic as a dominant source, emissions do not differ much between winter and summer and the higher concentration ratios are largely due to poorer dispersion conditions. Our cold/warm increases suggest that emission of components to which the DTT assay responds were fairly constant across seasons as well. The cold/warm ratio may be reduced compared to other pollutants, as OP DTT responds significantly to quinones and quinones are formed during photochemical transformation of PAH (Alam et al, 2013). There are few studies comparing OP levels between seasons. In an American study DTT levels between seasons in several locations differed less than in our study (winter/summer ratio = 1.2) (Vedal et al. 2013). Like Vedal et al., we used quartz filters for sampling and our extraction method was similar (high polarity solvent and filtration of the extract).

4. Conclusions

Significant spatial contrasts were found for OP DTT between 10 European study areas. The OP DTT levels were the highest in southern and the lowest in northern Europe. Our study conducted in 10 different European study areas supports a growing literature that OP DTT does not reflect large urban traffic contrasts. At street sites slightly higher OP DTT values were found than at urban background sites (median ratio 1.10). For five out of ten study areas LUR models could be developed for OP DTT with a relatively low explained variance (median R^2 = 33%). Overall, land use regression models did not effectively explain spatial variation of OP DTT possibly due to low levels of OP DTT and a lack of specific predictor variables. A model

combining all ten study areas resulted in a model with more specific predictor variables than the study-area specific models. In future studies more focus is needed on determination of additional OP sources not considered in our study including distant source areas and further optimization and standardization of OP sampling and analytical methods.

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