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▶ **To cite this version:**

Séverine Deguen, Laure Nicollet, Morgane Gilles, Arlette Danzon, Olivier Blanchard, et al.. Pregnancy Air Exposure: An R Package for Estimation of Exposure to Air Pollution during Critical Windows of Pregnancy. Open Journal of Statistics, 2017, 07 (03), pp.422-433. 10.4236/ojs.2017.73030 . hal-04028106

HAL Id: hal-04028106
https://ehesp.hal.science/hal-04028106

Submitted on 14 Mar 2023

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Scientific Research Publishing

Open Journal of Statistics, 2017, 7, 422-433
http://www.scirp.org/journal/ojs
ISSN Online: 2161-7198
ISSN Print: 2161-718X

Pregnancy Air Exposure: An R Package for Estimation of Exposure to Air Pollution during Critical Windows of Pregnancy

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How to cite this paper: Deguen, S., Nicollet, L., Gilles, M., Danzon, A., Blanchard, O., Le Nir, G., Zmirou-Navier, D. and Kihal-Talantikite, W. (2017) Pregnancy Air Exposure: An R Package for Estimation of Exposure to Air Pollution during Critical Windows of Pregnancy. *Open Journal of Statistics*, **7**, 422-433.
https://doi.org/10.4236/ojs.2017.73030

Received: January 25, 2017
Accepted: June 5, 2017
Published: June 8, 2017

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Abstract

Today, it is well known that ambient air pollution exposures may be related with different health outcomes including adverse birth outcomes (for instance, low birth weight and preterm birth). Then, researchers must estimate exposure to air pollution during different critical windows of exposure across pregnancy. In the literature, the most commonly examined critical windows of exposure are the first, second, and third trimesters of pregnancy, although the entire pregnancy is also studied. In this context, we developed an automatic procedure which estimates individual exposures by trimester. We illustrate usage of the ***Pregnancy Air Exposure*** package for all births within the city of Paris in 2011. Nitrogen dioxide data from monitoring stations and data modeled at the census block level were available from the air quality monitoring networks of Ile de France Region. Nitrogen dioxide, NO_2, has been chosen as an indicator of traffic-generated pollution. Newborn health data are available from the first birth certificate registered by the Maternal and Child Care department of Paris; more specifically, we used the date of birth and the gestational age to individually determine the beginning and the end of each trimester. The ***Pregnancy Air Exposure*** R package was created to simplify application of the procedure for non-specialists, and is freely available from the Equit'Area project website: (www.equitarea.org/documents/package_Exposure). The package contains two functions as well as the help files needed to run the procedure and yields air pollution exposure estimates by pregnancy trimester. The two functions can be used successively or independently according to the available in-

put data.

Keywords

Air Pollution Exposure, Pregnant Women, Critical Window of Exposure, R Software

1. Introduction

It is well documented that environmental exposures, and particularly ambient air pollution, may elicit adverse birth outcomes—including low birth weight and preterm birth [1]. This is of great interest in terms of public health, as preterm birth is also a predictor of both infant mortality and increased long-term morbidity in adulthood. Several epidemiological studies suggest that associations between air pollutants' concentrations and birth outcomes may vary, depending on the gestational age at which pregnant women are exposed [2] [3]. The most commonly examined critical windows of exposure are the first, second, and third trimesters of pregnancy, although the entire pregnancy is also studied.

For instance, whereas a number of epidemiological studies investigating associations between preterm birth and exposure to PM_{10} revealed increased risk during the third trimester only [4] [5] [6] [7] [8], some identified the entire period of pregnancy [4] [9], and others demonstrated an increased risk during specific trimester of pregnancy [10] [11] [12]. Similar results were found for low birth weight, with several studies demonstrating an increased risk with the rise of PM_{10} during the first or second trimesters while others showed an association when exposure was assessed over the entire pregnancy [7] [11] [13] [14] [15] [16]. This diversity of the epidemiological results demonstrates the need for additional studies in order to better characterize the critical window(s) of exposure and understand the biological mechanisms which might explain the differentiated increased risks of preterm birth and low birth weight across such window(s). To our knowledge, no automatic function facilitating reconstitution of air pollution exposure during pregnancy period exists. A procedure that aims to help the assessor to estimate individual exposures by trimester has been developed as part of the Equit'Area Project—a public health research program exploring social and environmental determinants of health inequalities in France. More precisely, one objective of the Equit'Area research is to study the air pollution adverse effect on the preterm birth and on the low birth weight, separately, and to investigate to what extend this association could be modify according to the level of neighborhood socioeconomic deprivation. The assessment of the individual exposure could represent a long and crucial process in this kind of epidemiological study. For this reason, we have developed a specific R package named Pregnancy Air Exposure, which is freely available from the Equit'Area project website: http://www.equitarea.org/documents/package_Exposure. The package contains both the functions and the help files needed to run the procedure and obtain

air pollution exposure estimates by pregnancy trimester. In this paper we explain the Pregnancy Air Exposure package and illustrate its use for births certificates in the city of Paris (France) in 2011.

2. Material and Methods

2.1. Data

Study area—The example data provided in the ***Pregnancy Air Exposure*** package concerns the city of Paris (capital). The spatial analysis unit of air pollution data is the sub-municipal French census block groups (called IRIS) defined by the National Institute of Statistics and Economic Studies (INSEE) whereas it is the newborn for the health event .With an average of 2,000 inhabitants, census blocks are constructed to be as homogeneous as possible in terms of socio-demographic characteristics and land use. The city of Paris is divided into 992 census blocks for a total population of approximately 2.23 million inhabitants, in an area of 105.40 km^2.

Air pollution data—Two types of air pollution data are routinely available: (1) data from monitoring stations and (2) data modeled by air quality monitoring networks of Ile de France Region (Airparif [17]).

1) Annual average ambient concentrations of nitrogen dioxide (NO_2) were modeled for each census block over the study period (2010-2011). The network used a deterministic model named ESMERALDA [18] which integrates various input parameters: meteorological data, emission sources and background pollution measurements. Selected emission sources were linear (main roads), surface (diffuse road sources, residential and tertiary emissions) or industrial point sources.

NO_2 has been chosen as the relevant pollutant for this study for several reasons:

- Firstly, ambient air NO_2 is considering being a good indicator of air pollution generated by traffic and other combustion sources [19].
- Secondly, it is also recognized that the spatial variability of the NO_2 distribution is higher than for other pollutant such as particulate matter PM10 or PM2.5.
- Thirdly, previous studies have demonstrated that exposure to dioxide may be related to adverse birth outcomes [2] [16] [20] [21] [22] and may also have direct toxic effects on the fetus [14].

2) Daily NO_2 concentrations were available from fixed monitoring stations (both from background and traffic stations) located within the city of Paris and available over the same period (2010-2011). A hierarchical agglomerative clustering was applied to associate each census block with a monitoring station. This clustering analysis allowed grouping census blocks and stations on the basis of similarities within a group and dissimilarities between different groups. Using this approach, each census block was assigned by Airparif to the monitoring station (named the "*index*" monitor) best representing overall NO_2 air quality within the census block (For more details, see Deguen *et al.* 2016 [23] and Kihal

et al. 2016 [24].

Health Data

Newborn health data are available from the first birth certificate registered by the Maternal and Child Care department of Paris (named PMI: Protection Maternelleet Infantile). This certificate is completed by parents and the health professional before exit of the maternity, within the 8 days following birth, then sent to the PMI local unit. Several mother and newborn characteristics are available from this certificate including birth date, gestational age and postal address of residency of the mother at the time when the certificate was completed, three crucial data needed to run the present package. All the postal addresses were geocoded at the level of residential census block.

For the purpose of this article, we illustrate our package on the births that occurred in the city of Paris between 1st January 2011 and 31st December 2011. Since the first birth certificate is a mandatory document handled by public health care services, data is considered exhaustive and covers quasi all registered births. In 2011 in Paris, 25,915 certificates have been transmitted to PMI, distributed over 936 IRIS. Between 1 and 107 newborns are found in each census block, with an average of 28 babies per census block. Their gestational age varies from 23 to 45 weeks with a mean of 39 weeks.

2.2. Air Pollution Exposure by Pregnancy Trimester

The procedure follows two independent and successive steps:

Step 1: *Daily reconstitution of air pollutant concentrations at the census block level.*

Daily concentrations of the pollutant in each census block were estimated based on the combination of the annual average concentration modeled in the census block with the relative daily variations to the annual average of its index monitor (as the index monitor is assumed to be representative of the daily variations of air pollution within the census block). For example, if, for a given day, the index monitor measured that daily concentrations of nitrogen dioxide were 10% lower than the annual average at this same location, the daily concentration in this census block is set 10% lower than its annual average concentration.

Step 2: *Calculation of individual air pollutant exposure by pregnancy trimester.*

For each birth, individual exposure to air pollution by trimester of pregnancy is estimated using the date of birth, the gestational age, and the census block in which the mother lived during her pregnancy, by averaging the indicator of daily concentrations of this census block over each trimester of pregnancy. The trimester divisions used are 1 - 13 weeks, 14 - 26 weeks, and equal or higher than 27 weeks to birth. If the gestational age is less than 26 weeks, the second trimester goes from the 14th week to birth. In order to take into account the fact that the trimester of pregnancy can last from one to 13 weeks, the procedure also gives the length of each trimester, which can be used as weights for respective

trimester exposures in a further statistical analysis.

3. Pregnancy Air Exposure Package

The package ***Pregnancy Air Exposure*** is available on the Equit'Area website and the installation is standard.

Pregnancy Air Exposure is composed of two main functions:

Reconstitution function creates the indicator of daily concentrations of the pollutant in each census block. Two data sets need to be specified: a data.frame containing the daily concentrations measured in each monitoring station and another with the annual concentrations and the index monitor of each census block throughout the study period (one year in the present case). The result obtained is a data.frame containing the estimations of the daily concentrations of the pollutant in each census block. This function is designed exclusively for air pollution data with no missing values. Yet, daily air pollutant concentrations collected in monitoring stations often contain missing values, which must consequently be imputed before using the ***Reconstitution*** function. To do so, the mtsdi package available on CRAN (https://cran.r-project.org/web/packages/mtsdi/index.html), can be used: the imputation obtained takes account for temporal dimensions, correlations between measurements in different monitoring stations, and the log-normality of the data (or normality if initial data distribution is already Gaussian) [25].

Trimester Exposure function calculates individual exposure by pregnancy trimester. It also requires two data sets: a data.frame with daily air pollution concentrations by census block (which can be the one obtained using the ***Reconstitution*** function), and a data.frame with births information. In the latter, there must be no missing values for the variables used by the function, *i.e.* the identification number, birth date, gestational age, and the census block where the mother lived. The result is the data.frame containing births data, with 8 new variables. Five of them contain exposure for trimester 1, trimester 2, trimester 3, trimesters 1 and 2, and the whole pregnancy, respectively. The 3 other variables contain the number of weeks of each trimester of pregnancy.

In both functions, other parameters exist if the variables names are not default ones (except for annual averages), or if the dates are not given in the standard R format (yyyy-mm-dd). It allows the user to choose the variable names or the date format that he/she may want to use. It also allows having the variables in any order in the data.frames.

4. Example

4.1. Descriptive Analyses of the NO_2 Distribution

Figure 1 represents the spatial distribution of the annual averages of NO_2 modeled at the census block level by Airparif for years 2010 and 2011. It shows that the annual concentrations of NO_2 are high on the whole city of Paris and is nearly always above the limit of 40 mg/m^3 defined by the European directive

[26]. It also exhibits the strong spatial heterogeneity of concentrations with a north/south gradient: NO_2 concentrations are generally higher in the north of Paris than in the southern census blocks.

Figure 2 reveals that, as expected, NO_2 concentrations measured by the traffic monitoring stations are always higher that those measured by the background stations (two stations have been selected for this illustration). Seasonal variabilities are also clearly visible with higher levels in winter and lower levels in summer, a seasonal pattern which is more evident for the background stations, less influenced by the continuous traffic emissions.

4.2. Application of the R Package

The package can be used with different spatial scales and for any air pollutant. Here is a complete example of the use of the package, for the city of Paris, at the census block scale and for nitrogen dioxide (NO_2).

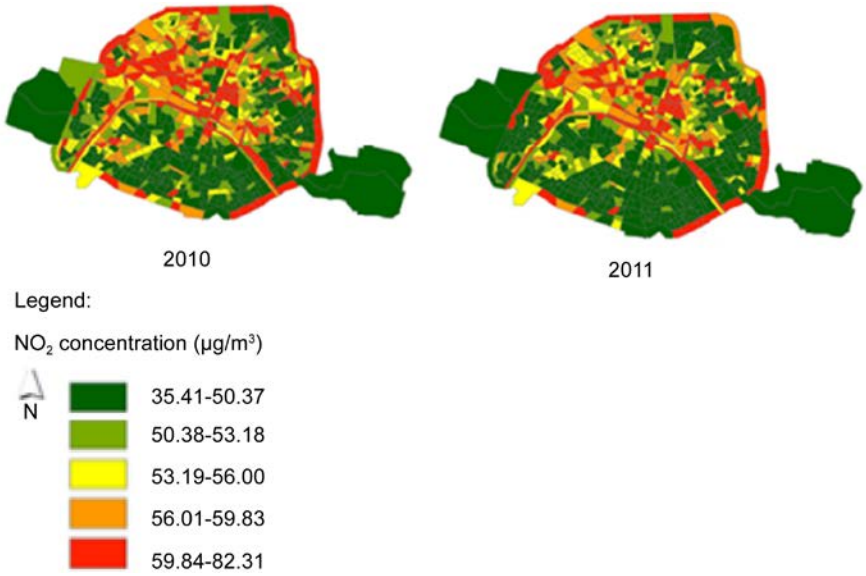


Figure 1. Spatial distribution of the annual averages of NO_2 modeled at the census block level by Airparif for years 2010 and 2011.

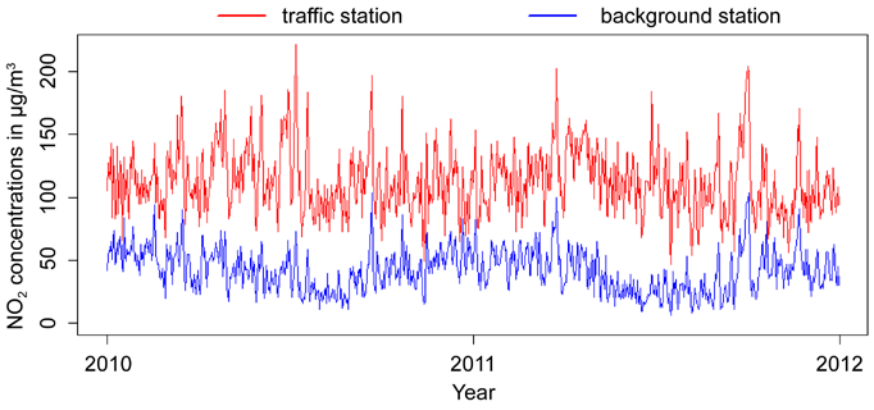


Figure 2. Daily NO_2 concentrations over years 2010-2011 in the city of Paris for a background (line colored in blue) and a traffic (line colored in red) monitoring stations.

After installing the package, it should be loaded with the R Software:

R > library (Pregnancy Air Exposure).

The first step consists in the reconstitution of daily NO_2 concentrations at the census block level.

Daily NO_2 concentrations measured by the monitoring stations in Paris should be first loaded:

R > data (daily NO_2 Monitoring Stations).

In order to load your own air pollution data, the read.table command can be used. Be aware that no missing values are accepted with the present R package; each year has to be complete from the 1st January to the 31st December. In the present example (Table 1), the data.frame contains 11 variables (one characterizing the dates and 10 qualifying the monitoring stations) and 730 observations (representing the total number of days for the 2 years, 2010 and 2011).

Annual averages and index monitors by census block must also be imported:

R > data (annual NO_2 Census Block).

You can load your own air pollution data using the read.table command, but these data need to verify the following conditions. The variables containing annual average of air pollutant have to be named "Mean_YYYY" (e.g. "Mean_2010"). Each spatial area must appear only once in this data.frame.

In our example, the data contains 4 variables and 992 observations. You find in Table 2 the first and last lines of the data.frame, with the average of NO_2 concentrations expressed in $\mu g/m^3$.

Table 1. Example of input data from the monitoring stations.

Date (dd/mm/yyyy)	AutA1	BASCH	BONA	BPAut	ELYS	PA06	PA07	PA12	PA13	PA18
01/01/2010	63	67	44	105	50	34	46	39	32	42
02/01/2010	109	81	72	127	82	49	53	61	54	53
03/01/2010	91	82	67	115	67	49	53	57	50	58
…	…	…	…	…	…	…	…	…	…	…
29/12/2011	89	53	54	98	80	27	30	31	26	30
30/12/2011	97	79	61	108	93	35	39	46	35	45
31/12/2011	76	47	49	94	67	24	28	28	23	30

Table 2. Example of input data modeled by air quality monitoring networks of Ile de france region.

censusBlock	Mean_2010	Mean_2011	indexMonitor
751010101	73.18447	68.76699	BONA
751010102	51.81188	52.50495	PA07
751010103	79.94667	74.60000	BONA
…	…	…	…
751208024	45.71287	43.97030	PA18
751208025	44.81159	43.36232	PA18
751208026	47.09210	45.78947	PA18

Then, the reconstitution at census block level can be done using the reconstitution function:

R > daily NO_2 Census Block <-
+ reconstitution (daily Concentrations by Monitoring Station =
+ daily NO_2 Monitoring Stations,
+annual Average and Index Monitor By Zone = annual NO_2 Census Block,
+ date VarName = "date",
+ date Format = "%d/%m/%Y",
+ zone VarName = "census Block",
+ index Monitor VarName = "index Monitor")

The two first parameters are the two data.frame imported at the previous step. Other parameters are needed if the variables names are not the default ones, or if the dates are not entered in the standard R format (*yyyy-mm-dd*). For example, here we use another date format (*dd/mm/YYYY*), and another name for the identification of the spatial unit ("*census Block*") than the default ones (with the parameters date Format and zone VarName). The index monitor and the name of the date (parameters date VarName and index Monitor VarName) are the default ones in our example (default values are given in the function help in R).The result, named *dailyNO$_2$CensusBlock,* contains the estimates of the daily NO_2 concentrations at the census block level expressed in μg/m^3, in a data.frame with 993 variables (the total number of census blocks) and 730 observations (Table 3).

Now, from the daily NO_2 concentrations for each census block, the procedure estimating exposure for each pregnancy trimester can begin.

First, birth data must be imported:

> data ("births").

When importing your own birth data, input data must contain at least the 4 following variables with no missing values (Table 4): individual identification number, date of birth, gestational age, and census block identification number where the mother live. Our birth data contains only these 4 variables, and 25,914 observations, which represent all births in Paris in 2011.

The first and last observations are the following ones:

Table 3. Extract of the result: each variable (except the date in the first column) corresponding to a census block.

Date (dd/mm/yyyy)	751010101	751010102	751010103	…	751208026
01/01/2010	50.59	53.67	55.26	…	45.00
02/01/2010	82.78	61.84	90.43	…	56.78
03/01/2010	77.03	61.84	84.15	…	62.14
…	…	…	…	…	…
29/12/2011	57.57	36.74	62.45	…	34.33
30/12/2011	65.03	47.76	70.55	…	51.49
31/12/2011	52.24	34.29	56.67	…	34.33

Table 4. Example of input health data.

id	censusBlock	birthDate	gestationalAge
1	751187205	27/02/2011	39
6	751186925	23/09/2011	40
16	751155703	06/10/2011	37
…	…	…	…
115087	751166103	20/10/2011	36
115088	751114114	18/08/2011	37
115091	751208008	19/06/2011	41

Finally, trimester exposures can be estimated:

> exposures<- trimester Exposure(
+ daily Concentrations = daily NO_2 Census Block,
+ births = births,
+ id VarName = "id",
+ birth Date VarName = "birth Date",
+ gestational Age VarName = "gestational Age",
+ zone VarName = "census Block",
+ date VarName = "date",
+ date Format = "%Y-%m-%d",
+ birth Date Format = "%d/%m/%Y").

The two first parameters are air pollution data and birth data. As the previous function, the trimester Exposure function provides other parameters to use other variables names or dates formats than the default ones. Format of the exposure date and birth date variable can be changed. It is important that the user verifies that all the dates are compatible: exposure dates must cover the births dates period, and one year before to cover the period of pregnancy. In this example, we use birth data in 2011; for this reason, the period of air pollution data must go from 2010 to 2011 in order to estimate exposure of a birth occurring in the beginning of year 2011.

The result of this function is the data.frame containing births data, and the 8 new variables described before (Table 5). The first and last rows for these new variables are:

If pregnancy lasts less than 27 weeks, the observation will look like: (with "NA" representing a missing value)

T1	T2	T3	T12	T123	nWeeksT1	nWeeksT2	nWeeksT3
62.94	34.43	NA	49.88	NA	13	11	NA

The second function computing trimester exposures can be used on its own, "for different exposure assessments. As an example, the census block attributed to each birth can be replaced by a monitoring station (probably the closest station from where the mother lives), and pollution data in the first parameter by

Table 5. Example of exposure during different critical window.

T1	T2	T3	T12	T123	nWeeksT1	nWeeksT2	nWeeksT3
36.65	48.88	61.39	42.76	48.97	13	13	13
52.58	56.52	48.19	54.55	52.3	13	13	14
57.03	41.47	42.47	49.25	47.20	13	13	11
…	…	…	…	…	…	…	…
52.94	55.69	59.94	54.32	56.28	13	13	10
55.37	53.47	60.31	54.42	56.48	13	13	11
57.77	34.58	38.80	46.18	43.59	13	13	15

Legend: T1: daily average exposure during the first trimester; T2: daily average exposure during the second trimester; T3: daily average exposure during the third trimester; T12: daily average exposure during the first and second trimester; T123: daily average exposure during the whole pregnancy; nWeeksT1: number of weeks of the first trimester; nWeeksT2: number of weeks of the second trimester; nWeeksT3: number of weeks of the third trimester. *Note*: *The last newborn presented in this table was exposed during the* 15 *weeks of his last trimester of gestation to an average of* 38.80 $\mu g/m^3$ *of* NO_2 *per day. He/she was exposed during the* 41 *weeks of gestation to an average of* 43.59 $\mu g/m^3$ *of* NO_2 *per day.*

daily concentrations, by monitoring stations instead of census blocks. In this case, the value given to daily Concentrations parameter in trimester Exposure function would look like the data.frame daily NO_2 Monitoring Stations. For this purpose, all the variable names can be changed in the parameters of the functions.

5. Conclusion and Perspectives

In this article we have presented the ***Pregnancy Air Exposure*** package designed to ease the estimation of exposure to air pollutants during three windows across pregnancy trimesters. To our knowledge, no such reproducible procedure had previously been proposed. One advantage of the package is that the two implemented functions can be used independently. For instance, if input data are already in the appropriate format, the first function is not needed, and exposure during pregnancy periods can be readily estimated. As a domain of application for future work, the package could be used to extend estimation of air pollution to pre-pregnancy—during the conception period, for instance. Lastly, we expect to extend the package in the future, such as implementing complementary functions and additional tools that would allow visualization of results (such as mapping). These improvements will be made in response to user feedback and requirements.

Acknowledgements

This paper was supported by the following grant(s): Fondation de France 201300040943 2013-2016 to Séverine Deguen.

This work is supported by Fondation de France (grant N° 201300040943 2013-2016) and the EHESP School of Public Health. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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