SEVENTH FRAMEWORK PROGRAMME

HEALS

Health and Environment-wide Associations based on Large population Surveys

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http://www.heals-eu.eu/

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WP9 Exposure Monitoring Throughout Lifetime – Constructing the Exposome

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1 Introduction

The Health and Environment-wide Associations based on Large population Surveys (HEALS) project is funded under the European Union's Seventh Framework Programme (grant agreement No. 603946). It aims to develop and test methods to characterize the human exposome, which is defined as the totality of exposures from conception onwards. This is a broad concept, and HEALS will approach its study using various methods to examine the exogenous and endogenous exposures and modifiable risk factors that predispose a person to disease. The project will employ various "–omics" technologies to determine internal biomarkers and relate these to environmentally mediated disease using bioinformatics and biokinetic and systems biology modeling. Additionally, the study will test two new methodologies for evaluating the external exposome: Part A) the use of new sensor and other "low-cost" commercial technologies in collecting exposure information and filling data gaps characteristic of conventional monitoring technologies; and Part B) the use of agent based modelling and hierarchical clustering methods for modeling life trajectories. The HEALS approach will be applied in several existing cohort studies of various chronic disease outcomes and also in a prospective birth cohort study, of both twin and singleton births, in several European countries (EXHES study). The two parts of the methodology for the external exposome will be presented as D9.2, Part A (present document) and then D9.2 Part B, which will be a follow-on document.

Work package 9 (WP9) of HEALS has conducted two pilot studies to test a sensor based exposure assessment protocol that informs the design and implementation of the EXHES study. The objective of the pilot study was to develop a protocol for measuring external environmental exposures and related factors using a non-targeted, data driven approach, where investigators gather data with the aim to do exploratory analyses to discover associations that lead to further, more targeted hypothesis driven research. Since the exposome is meant to include the totality of all exposures and factors that influence these exposures, a methodology for measuring the external exposome must therefore include numerous pollutant concentrations in air, water, food, etc. and other environmental factors such as UV exposure from sunlight. Aspects of the environment that can influence health and exposure should also be included, such as personal activity, location, diet, and demographic and socioeconomic factors. A wide variety of personal exposures can be constructed based on these aspects, combining data from personal monitoring and external datasets, as well as modeling methods such as agent-based modelling. This document describes the preliminary results of the WP9 pilot, including some descriptive results of the data, and the implementation experience for each center. From this, a recommendation for methods to estimate the exposome in cohort studies (both prospective and retrospective) will be made, including methods for extending the assessment longitudinally.

2 Summary of WP9 Sensor Pilot methods

Two pilot studies were performed – a "pre-pilot" which investigated in greater detail sensor-based methods for gathering data on location and physical activity; and a field pilot of multiple sensor technologies along with other methods of exposure assessment. The pre-pilot involved researcher participants in 7 cities across Europe and the field pilot involved families with young children in 3 countries. Results from these pilots provide recommendations for the use of sensor technology in exposure and epidemiology studies for characterizing the exposome. The pre-pilot methods and results will be described first and then the field pilot methods and results.

2.1 Pre-pilot

The first pilot study evaluated the utility of the MOVES smartphone app to determine a person's location, including whether they were inside or outside and in transport, and the use of the Fitbit Flex to measure a person's physical activity levels. Additional sensors were added for validating the MOVES app and Fitbit and also to see if the predictive power of these devices could be improved by gathering additional information.

2.1.1 Methods

Study subjects included 4 researchers from each of 7 cities across Europe (Figure 1).

Figure 1: City locations for the pre-pilot (Edinburgh, Utrecht, Stuttgart, Zagreb, Kozani, Athens, Thessaloniki)

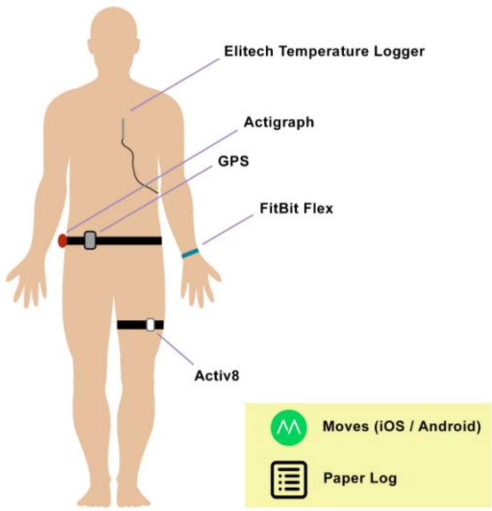
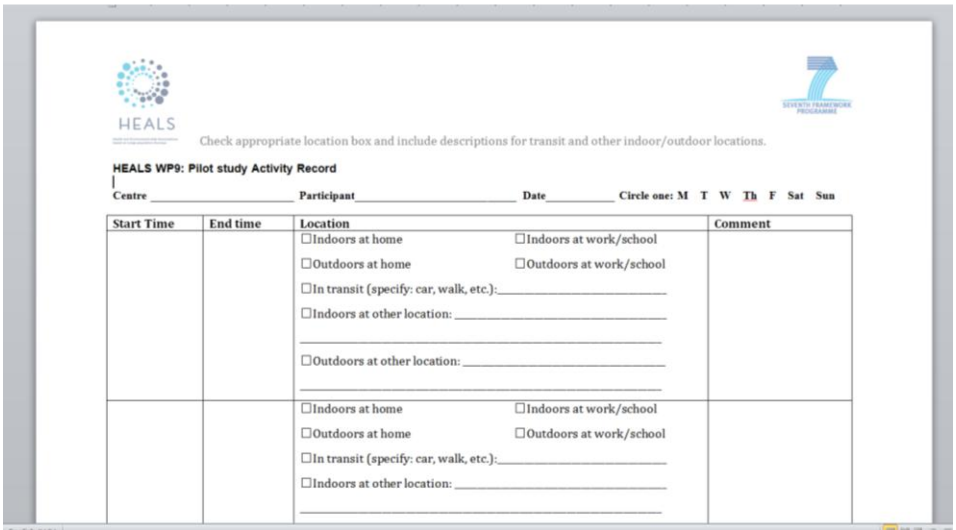


Figure 2: Devices worn or carried during the pre-pilot

Each researcher (Figure 2) carried a smartphone with the MOVES app, a temperature monitor, and Actigraph monitor, a GPS (Qstarz), and filled out a paper log (Figure 3) with their location/activity information for about 7 days. A subset of researchers also carried a UV meter. The temperature and UV meters were carried as additional information hypothesized to improve estimates of whether a person was inside or outside.



HEALS

Check appropriate location box and include descriptions for transit and other indoor/outdoor locations.

HEALS WP9: Pilot study Activity Record

Centre ____________ Participant ____________ Date ________ Circle one: M T W Th F Sat Sun

Start Time	End time	Location	Comment
		☐Indoors at home ☐Indoors at work/school ☐Outdoors at home ☐Outdoors at work/school ☐In transit (specify: car, walk, etc.):________ ☐Indoors at other location: ________ ☐Outdoors at other location: ________	
		☐Indoors at home ☐Indoors at work/school ☐Outdoors at home ☐Outdoors at work/school ☐In transit (specify: car, walk, etc.):________ ☐Indoors at other location: ________	

Figure 3: Paper time activity log

2.1.2 Results

Analyses to date have included comparisons of data from MOVES with the paper log and GPS, data from Fitbit with Actigraph, and models to incorporate additional information from the temperature

and UV meters and other environmental information (e.g. time-of-day, weather) to predict times spent indoors, outdoors, and in transport.

2.1.2.1 MOVES and paper log

An analysis of MOVES and paper log data from all data found that MOVES was accurate 89% of the time, with the paper log considered the reference (Table 1).

Table 1: Cross tab for the MOVES app versus the paper log (minutes)

		MOVES							
		Cycling	***Home***	***Place***	***Work***	***Transport***	***Outdoor***	***Walking***	***Total***
Paper log	***Cycling***	419	21	48	0	142	0	33	663
	Indoor	68	86,210	35,044	7,646	1,660	125	437	131,190
	Motorized	1	793	561	55	5,261	9	119	6,799
	Outdoor	324	1,479	6,113	63	271	461	1,960	10,671
	Walking	37	347	870	169	275	18	2,087	3,803
	Total	849	88,850	42,636	7,933	7,609	613	4,636	153,126

The sensitivity of the MOVES app compared to paper log was high (86) for 'Indoor', moderate (47-59) for 'Motorized', 'Walking' and 'Cycling' and low (4) for 'Outdoor'. The specificity was high (>90) for all categories except for 'Indoor' (59) (Table 2).

A comparison of location and activity from the MOVES App compared to the paper log for two different participants in Athens is shown in Figure 4. In general, the MOVES App is able to record user's location adequately. The main advantage of using the MOVES App is that self-reporting is not required, as well as the smooth transition between several locations in a short period of time, which is not always possible with the paper log. MOVES has a key advantage over paper recording in that the participant does not need to have any regular requirement to record the information which is automatically generated by the app. However, according to the paper log, it was observed that using MOVES, there may be inaccuracies in the determination of location when a person goes between short distances and it is unable to determine whether an individual is indoors or outdoors. As it is shown in Figure 4, the App recognizes that the participant is at home, but does not distinguish the difference between indoors and outdoors (also reflected by the very low sensitivity), while using the paper log this information can be obtained. MOVES does have the functionality where the user can correct or annotate the location and transport information, and this feature could improve the accuracy of MOVES.

Table 2: Sensitivity (true positive estimation / (true positive estimation + false negative estimation), specificity (true negative estimation / (true negative estimation + false positive estimation) and precision (true positive estimation / (true positive estimation + false positive estimation) of the MOVES app versus the paper log

		Cycling	Indoor	Motorized	Outdoor	Walking	Average
Only MOVES	**Sensitivity**	59	86	68	4	47	53
	Specificity	100	59	99	100	99	91
	Precision	49	92	69	75	45	66

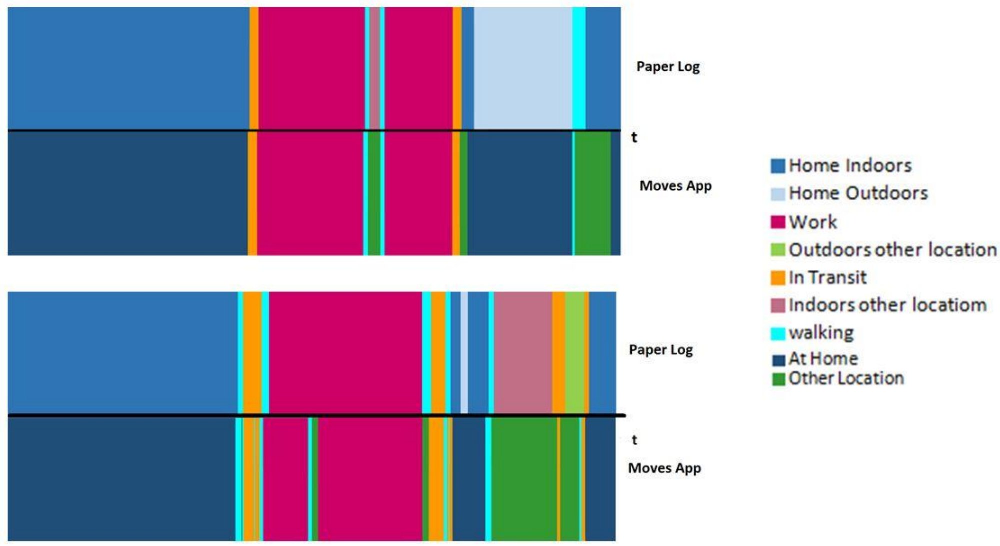


Figure 4: A comparison of time spend in various locations according to MOVES and the paper log for two Athens participants

2.1.2.2 Random forest analyses

Random forest models were constructed to evaluate if additional information could inprove the MOVES classifications. Variables included were: MOVES output variables, Day of the week, hour of the day, distance to nearest highway, distance to nearest railway based on MOVES GPS location, number of steps (Fitbit). These variables were selected because these can be obtained from the pilot study dataset. In addition, a separate model was constructed in which Temperature on the person (personal sensor) was added. Table 3 and Table 4 show the cross tabs for the output of these models versus the paper log and Table 5 shows the sensitivity, specificity and precision of these models. The random forest models were adjusted for over performance due to the many repeated measurements per person.

Table 3: Cross tab for the Random forest model (MOVES output plus information available in the pilot study) versus the paper log

		Predicted by random forest (incl. temp)					
		Cycling	*Indoor*	*Motorized*	*Outdoor*	*Walking*	*Total*
True (logbook)	*Cycling*	216	6	239	327	241	1,029
	Indoor	5	14,830	964	7,892	896	24,587
	Motorized	11	662	9,590	1,874	679	12,816
	Outdoor	304	1,607	873	12,570	4,071	19,425
	Walking	5	390	1,058	2,199	4,154	7,806
	Total	541	17,495	12,724	24,862	10,041	65,663

Table 4: Cross tab for the Random forest model (MOVES output plus information available in the pilot study AND Temperature) versus the paper log

		Predicted by random forest (excl. temp)					
		Cycling	*Indoor*	*Motorized*	*Outdoor*	*Walking*	*Total*
True (logbook)	*Cycling*	41	146	420	613	579	1,799
	Indoor	0	12,119	1,865	9,560	1,296	24,840
	Motorized	26	764	11,700	1672	749	14,911
	Outdoor	55	3,371	1,179	15,779	4,107	24,491
	Walking	11	669	841	3,407	4,864	9,792
	Total	133	17,069	16,005	31,031	11,595	75,833

Table 5: Sensitivity (true positive estimation / (true positive estimation + false negative estimation), specificity (true negative estimation / (true negative estimation + false positive estimation) and precision (true positive estimation / (true positive estimation + false positive estimation) of the MOVES app and random forest models versus the paper log.

		Cycling	Indoor	Motorized	Outdoor	Walking	Average
Only MOVES	Sensitivity	59	86	68	4	47	53
	Specificity	100	59	99	100	99	91
	Precision	49	92	69	75	45	66
RF incl. temp	Sensitivity	21	60	75	65	53	55
	Specificity	49	36	42	30	42	40
	Precision	40	85	75	51	41	58
RF excl. temp	Sensitivity	2	49	78	64	50	49
	Specificity	49	36	41	28	42	39
	Precision	31	71	73	51	42	54

The additional information in the random forest models resulted in an improved sensitivity for the categories that resulted in the lowest sensitivities when estimated with the MOVES app: Outdoor and Motorized transportation. Especially Outdoor had a greatly improved sensitivity (Table 5). However, (as can be expected) this was at the cost of the specificity and precision for these categories. For both categories there was no difference between the random forest model with and without Temperature. The random forest model resulted in lower overall accuracy of the prediction of cycling and indoor compared to the MOVES app alone (sensitivity, specificity and precision). Adding Temperature to the model greatly improved all indicators of accuracy but not to the level of only MOVES. Ongoing work is focused studying the effect of using these methods (MOVES versus machine learrning) on misclassification of estimated cumulative exposure to environmental agents.

It should be noted that the effect of Temperature in this study is quite low due to the season in which the prepilot was held. Contrast in Tempartue on the person was suboptimal with high outdoor temperature levels Figure 5 shows that the the distribution of personal temperature measured indoor vs outdoor as indicated on the paper log).

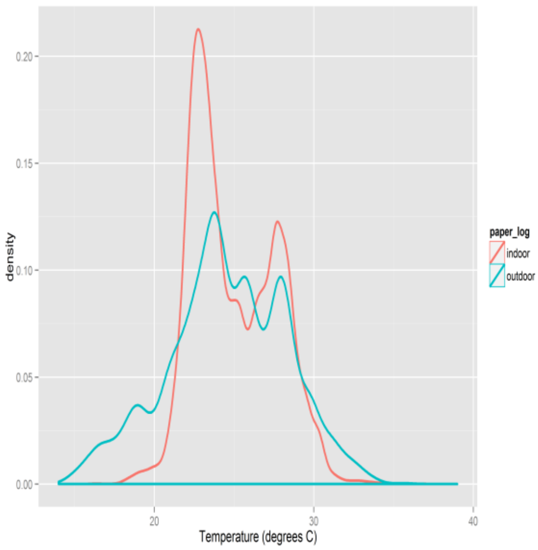


Figure 5: Personal temperature indoor and outdoors

2.1.2.3 Fitbit, MOVES and Actigraph

Figure 6 shows a comparison between Fitbit steps and MOVES App steps for a single participant in Athens during the week of the campaign, while Figure 7 illustrates a scatter plot of MOVES App versus Fitbit total steps per day for a subset of the participants in Athens. As shown, the MOVES App tends to underestimate step counts compared to the Fitbit Flex, probably because of the participant's difficulty in carrying the mobile phone all the time, with respect to the Fitbit Flex that it can be worn on the wrist and record the activity in continuous basis. It was found that the mean relative percent difference between these two methods was 53%. Similar results were obtained when the MOVES App steps counts were compared to those from the Actigragh device. Daily total Fitbit and Actigraph steps were compared using Pearson's Correlation Coefficient and the analyses

for a subset of the volunteers showed a good concordance (0.87), with the Actigragh in general tended to systematically underestimate the Fitbit steps (Figure 7).

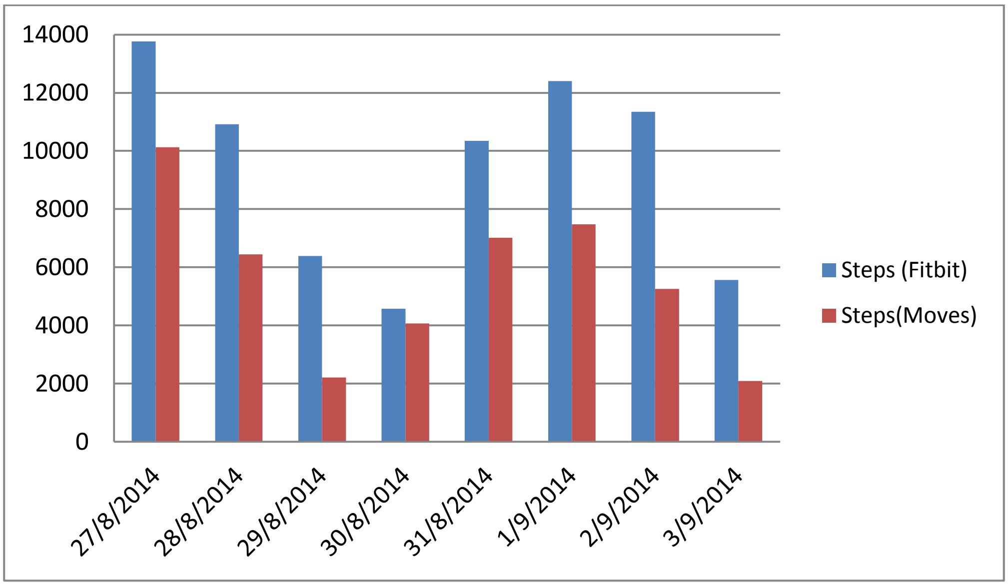


Figure 6: Comparison between Fitbit steps and MOVES App steps for a single participant in Athens during the week of the campaign.

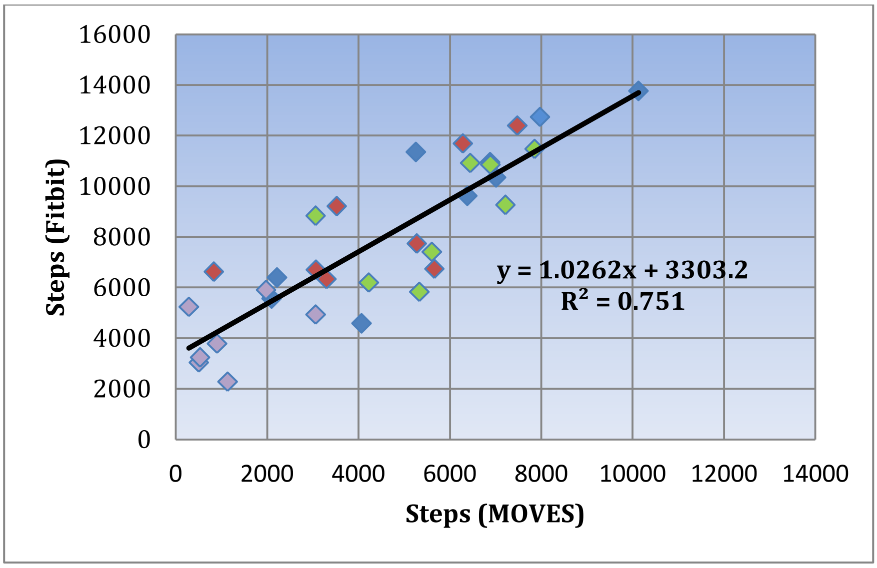


Figure 7: Scatter plot of total steps per day for MOVES App versus Fitbit. Different colors indicate data for each participant in the Athens subset

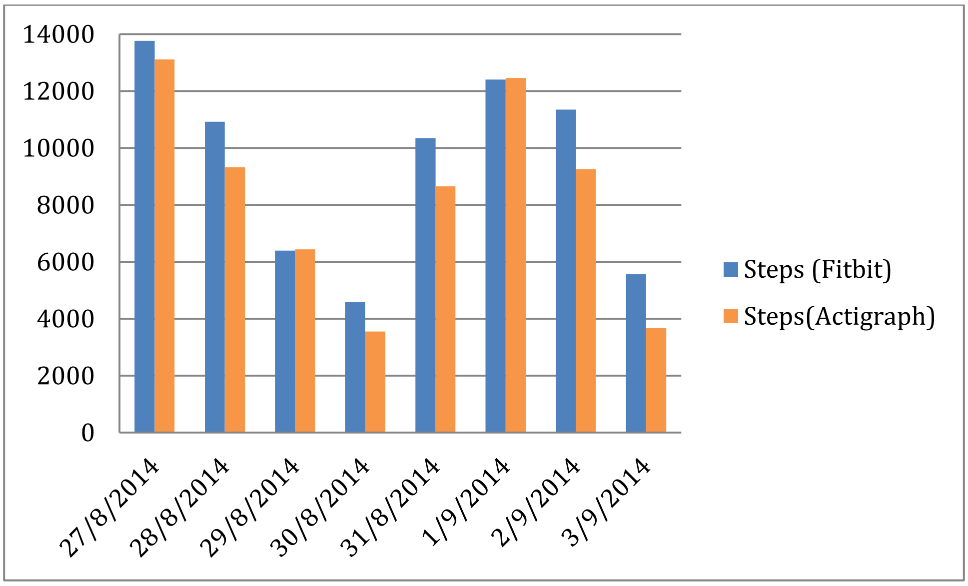


Figure 8: Comparison between Fitbit steps and Actigraph steps for a single participant in Athens during the week of the campaign.

We were additionally able to download the minute-by-minute step count data from the Fitbit. We aggregated the steps by hour, as the data were not consistently measured on a minute basis between Actigraph ("gold standard") and Fitbit. From Figure 9, we can see that the relationship between the two devices appears quite good, but when we look at Figure 10 we see that the fit degenerates at lower step counts. Aggregating up to a day improves the fit between the two devices (Figure 11).

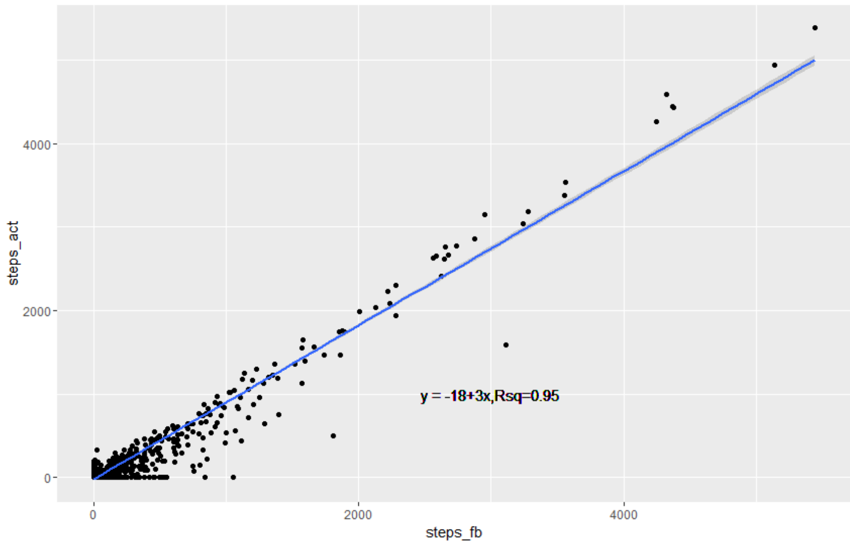


Figure 9: Concordance of Fitbit vs. Actigraph minute-by-minute steps for Edinburgh participants

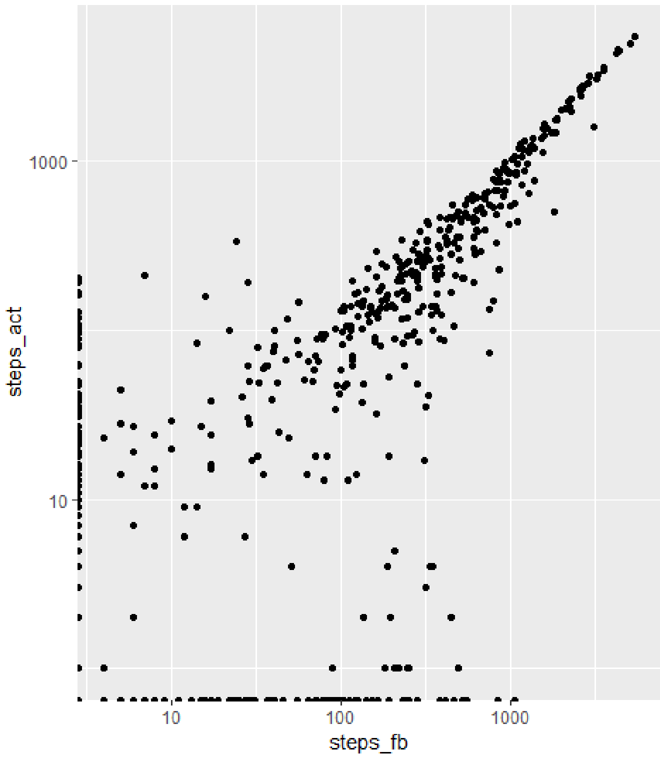


Figure 10: For Edinburgh, relationship between steps recorded with Actigraph and Fitbit on an hourly basis log transformed

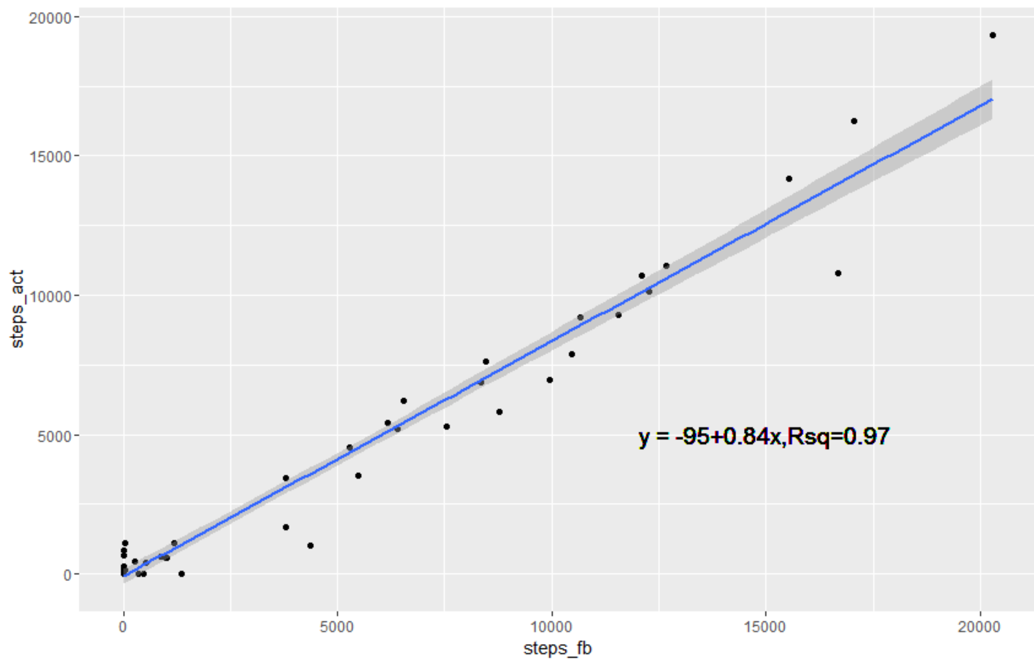


Figure 11: For Edinburgh, relationship between daily step counts recorded by Fitbit vs. Actigraph

2.2 Field pilot methods

The study aims to characterize children's exposure by measuring the place(s) that they spend the most time in (assumed to be the home) and by examining the exposure of their primary caretaker or guardian. It is assumed that the environmental exposure of their primary caretaker or guardian will be closely related to the child's exposure. Each city (or city cluster) recruited households with at least one child ≤ 3 years old. For each household, one adult (the primary caretaker for the child in the study) and one child was enrolled into the study (in some cases both parents were enrolled). Monitoring took place over approximately 5 days, including a weekend. Researchers visited the family on the first day to set up equipment, do initial surveys, and provide instructions and questionnaires to the participants, and on the last day to remove the monitoring equipment and retrieve questionnaires that were left with the participants to answer.

The data collected in the study is summarized in Table 6.

Table 6: Data collection methods

Factor	Device	Monitoring location	Data collected	Data resolution
Sensor based apps ("low-cost" commercially available technologies)				
Physical activity	Fitbit	Personal, worn on guardian's wrist	Number of steps	By minute
Location	MOVES app (on phone)	Personal, carried by guardian	Latitude and longitude for various locations person visits; steps; transport	Timestamp to minute, but not regular collection intervals
Air temperature – indoors	Netatmo	Indoor at home, main living area and child's bedroom	Temperature in Celsius	Timestamp to minute, but not regular collection intervals
Humidity – indoors	Netatmo	Indoor at home, main living area and child's bedroom	Relative humidity as %	Timestamp to minute, but not regular collection intervals
CO_2 – indoors	Netatmo	Indoor at home, main living area	CO_2 levels in ppm	Timestamp to minute, but not regular collection intervals
Noise in the home	Netatmo	Indoor at home, main living area	Noise levels in dB	Timestamp to minute, but not regular collection intervals

Factor	Device	Monitoring location	Data collected	Data resolution
Noise	Widenoise Plus app	Personal, installed on guardian's phone	Noise in dB as recorded by phone; person's rating of noise	Momentary (e.g. single point in time) and at non-regular intervals– requires person to actively take sample and rate it
Particulate matter	Dylos DC1700	Main living area	Number of particles >0.5 µm and >2.5 µm in size diameter	Minute
Dietary data (including water and other drinks)	Fatsecret app	Personal, installed on the guardian's phone (recorded by guardian for guardian and child)	Type of food eaten, amount eaten, meal eaten	Several times a day
Consumer products	Redlaser app; phone camera	Personal, installed opn guardian's phone (recorded by guardian for guardian and child)	Barcodes and pictures of products used for cleaning and personal care	No time aspect
Non-sensor samples				
Dust	Dust from vacuum cleaner	Home indoor	Entire dust sample from home vacuum	Integrated over several days (duration unknown)
Dust deposition	Dust settled onto electrostatic sheet	Home indoor	Sampler placed in home, may be analyzed for allergens, etc.	Integrated over 5 days or 2 weeks (depends on city)
Questionnaires*				
Building/area characteristics	Fieldworker conducted survey	Home indoor and outdoor environs	Survey answers	General – applicable to current or previous times
Indoor home activities	Fieldworker conducted survey	Home indoor	Survey answers	General – applicable to current or previous times
Socioeconomic status	Questionnaire (self-administered by guardian)	Personal/family	Survey answers	General (includes residential history)
Noise (2 questionnaires)	Fieldworker conducted	Personal and at home	Survey answers	1^{st} visit (general)

Factor	Device	Monitoring location	Data collected	Data resolution
	survey			2nd visit (week of monitoring)
Electromagnetic fields	Questionnaire (self-administered by guardian)	Personal, applicable to all members of family	Survey answers	General
User experience	Questionnaire (self-administered by guardian)	Personal	Survey answers	Monitoring period

*Each center may have used different approaches to administer these surveys, therefore “Device” field may be different by center. For example, in some centers the fieldworkers may have given all questionnaires to participants to fill out on their own time.

Each center added on various complementary measurements, for both device comparison and additional data collection. These are detailed in the next sections.

2.2.1 Additional methods

These were not all the same, but some methods attempted to do similar things across all cities. These are described here.

In particular, all cities did additional comparison monitoring between the Dylos, which measures particle number concentration (PNC) and a method of measuring particle mass concentration as a means of converting the Dylos count data to mass concentrations, the metric that health based standards for particulate matter are based on. There are two potential methods to be used for this conversion:

- Method 1 is based on assumptions that the particles are spherical and of a particular density, therefore the mass of the particles of a specific diameter are calculated using the equation:

$$\text{Total mass} = \sum \pi\, \rho\, PNCbin \frac{d^3{}_{bin}}{6} \qquad (1)$$

- Method 2 is an empirical calibration based on a statistical model fit between co-located measurement between the reference monitor and the Dylos. In this deliverable a single method using an empirical calibration from a previous study was used to do a preliminary calculation of the fine particle (PM2.5) concentrations, but analyses are being done to determine the best calibration for each city.

2.2.1.1 Netherlands

Noise

An additional app to measure noise (Spectrum Analyser) was used in 50% of the Dutch households.

Conversion of the Dylos data to mass

In 2 additional field surveys a method was developed to convert PNC to PM2.5 mass using the methods described above.

Dylos has only one size bin in the PM2.5 range, resulting in inaccuracy when applying Equation 1. In the literature methods are described for converting the PNC obtained by Dylos to mass (Dacunto et al., 2015; Semple et al., 2013a). In these previous studies the Dylos was run side by side with a high cost reference particle counter that covers a range of size bins within the PM2.5 range in an experimental setup with a known PM source (cooking and second hand cigarette smoke). A calibration curve was then fited for the calculated PM2.5 mass obtained by the reference device on the PNC count from the Dylos. The calibration curve can be used to convert overall PNC counts to PM2.5 mass. The following two additional field surveys were conducted to apply this method in the HEALS study:

1. Fitting a calibration curve in a field setting

   In 3 Dutch homes the (real time) aerodynamic particle sizer (APS, TSI USA) which counts PNC in 22 size bins in the PM2.5 range was run side by side with the Dylos for 3-5 days. PM2.5 mass was calculated based on Equation 1 and a calibration curve was fit to the Dylos counts.

2. External validation of the methodology

   In 5 Dutch homes the Dylos was run for 5 consecutive days. In parallel five 24h gravimetric samples were collected using the Harvard Impactor. 24h PM2.5 concentrations were calculated by applying the fitted curves obtained by this study and obtained by the two previous studies for the relevant time periods and compared to the filter weights.

2.2.1.2 UK

PM2.5 comparison: Harvard Personal Environmental Monitors were used to measure $PM_{2.5}$ gravimetrically in 10 households. The samplers were located in the main living area of the family home out of reach for children. The sampling time was approximately 24 hours at a sampling rate of 4 liters per minute. The 24 hour averages are used to compare with the Dylos data, similar to that done with the Harvard Impactors in the Netherlands.

Cleaning product usage: Families were asked to choose 1-3 cleaning products that they would use several times a week. These products were labelled with a sticker on which the dates of the pilot week were printed. The participants were asked to tick off the date when they used the respective product.

2.2.1.3 Greece

The field campaigns in Greece were conducted in Athens and Thessaloniki, the two major cities. Beyond the basic instrumentation additional monitors were placed in the main living area of the residences, in order to obtain more information on indoor air pollutants (Table 2).

Table 7: Additional devices used in Greece

Factor	Device	Monitoring Location	Data Collected	Data Resolution	Number of Houses
Particulate Matter	Grimm 1.108 (Grimm Aerosol, Germany)	Main living area	Mass of Particles 0.23-20µm (16 channels)	Minute	7 in Athens
Particulate Matter	Aerocet 531S	Main living area	Number of Particles 0.5, 1.0, 5.0, 10.0 µm in size diameter	Minute	6 in Athens 4 in Thessaloniki
TVOCs	AQ monitor (AQ monitors, UK)	Main living area	TVOCs levels in ppb	By 15 minutes	13 in Athens 3 in Thessaloniki
CO	AQ monitor	Main living area	CO levels in ppm	By 15 minutes	13 in Athens 3 in Thessaloniki
NO	AQ monitor	Main living area	NO levels in ppb	By 15 minutes	13 in Athens 3 in Thessaloniki
NO_2	AQ monitor	Main living area	NO2 levels in ppb	By 15 minutes	13 in Athens 3 in Thessaloniki
CO_2	AQ monitor	Main living area	CO2 levels in ppm	By 15 minutes	13 in Athens 3 in Thessaloniki
Air Temperature-Indoors	AQ monitor	Main living area	Temperature in Celsius	By 15 minutes	13 in Athens 3 in Thessaloniki
Relative Humidity-Indoors	AQ monitor	Main living area	Relative Humidity as %	By 15 minutes	13 in Athens 3 in Thessaloniki
NO_2	Aeroqual Series 500 (Aeroqual, NZ)	Main living area	NO2 levels in ppb	By 5 minutes	13 in Athens 2 in Thessaloniki
O_3	Aeroqual Series 500	Main living area	O3 levels in ppm	By 5 minutes	13 in Athens 6 in Thessaloniki
BTX, Aldehydes	Radiello Passive Samplers	Main living area	BTX and Aldehydes levels in ppb	Monitoring period	8 in Athens

2.2.2 Data management

Data from the different types of instruments (Table 6) were collected into different repositories, which are then merged into the HEALS Geodatabase (WP12) in a secure, user and password protected area, for access to specified HEALS researchers. Wireless device collected data was housed in the HEALS portal, developed at TNO; some questionnaire data was entered via tablet using the ODK software; remaining questionnaire data (generally ones filled out by participant) were entered into an Excel datasheet; Dylos particle count data were downloaded from the instrument directly, and samples for analysis were logged and stored.

2.2.2.1 Data portal

An online portal was developed to collect the data obtained with the wireless devices and apps (Fitbit, Netatmo, Fatsecret app, MOVES app) via API's. The data was directly stored in the portal database. Participants had to provide their permission for the portal to access their data from the apps/devices. The portal also had an interface for the participants on which they could view their data collected by the devices.

2.2.2.2 Open Data Kit data

The Open Data Kit (ODK) was used to develop a mobile device version of the questionnaires for use in the field (https://opendatakit.org/). Tablets were used either by the fieldworker while administering the questionnaires to subjects or as a means of data entry, in cases where the tablet version was not yet finalized for use in the field. The data entered was then stored in an online database which could be downloaded as a .csv file.

3 WP9 Field pilot results

3.1 Overall summary results

The pilot study was completed at varying times, with Netherlands being completed in autumn 2015, UK in spring 2016, and Greece in summer 2016. Analyses of data are ongoing, but here we summarize the data collected. Table 8 and Table 9 show summaries of the raw data immediately available from the sensor devices. Temperature, relative humidity, noise, and particle count data are in the same units reported by the instrument. Because these data are raw distributions, it is recognized that data, particularly at the lower limits, may represent the error at the detection limits of the instruments and likely require further processing. Data cleaning is underway to generate the final datasets for further analyses. Particle counts were converted to mass concentration using the equation in Semple (Semple et al., 2013b) as a preliminary estimate. However, because the Semple model includes homes with second-hand smoke, it may not be an accurate calibration. Investigation is ongoing to determine if more specific calibrations can be developed for each city based on the additional data collected (Section 2.2.1.1).

Table 8: Netatmo raw results by country

Parameter	Country	Number subjects	Minimum	Median	Mean	Maximum
Temperature (°C)						
	NL	50	14	22	22	34
	UK**	29	15	18	19	24
	GR1	25	21	27	27	38
	GR2	25 (winter: 6, summer: 19)	11 (winter) 18(summer)	20 (winter) 23 (summer)	20 (winter) 23 (summer)	29 (winter) 34 (summer)
Humidity (%)						
	NL	50	31	55	55	98
	UK**	29	50	62	63	81
	GR1	25	23	46	48	75
	GR2	25 (winter: 6, summer: 19)	29 (winter) 33(summer)	50 (winter) 58 (summer)	50 (winter) 58 (summer)	72(winter) 88 (summer)
Carbon dioxide (ppm)						
	NL	39	1	575	562	2462
	UK**	29	419	757	879	2618
	GR1	25	296	641	693	3418
	GR2	25 (winter: 6, summer: 19)	292 (winter) 277 (summer)	899 (winter) 619 (summer)	993(winter) 860 (summer)	2938 (winter) 4996 (summer)

Noise (dB)						
	NL	50	33	53	51	78
	UK**	29	47	51	52	70
	GR1	25	37	42	42	56
	GR2	25 (winter: 6, summer: 19)	35 (winter) 35 (summer)	38 (winter) 39 (summer)	41 (winter) 41 (summer)	77 (winter) 75 (summer)

**Values shown are based on household means

Table 9: Particle results by country

Parameter	Country	Number subjects	Minimum	Median	Mean	Maximum
Particle count (>0.5 µm), (particles/cubic foot of air)						
	NL	52	200	84800	165400	6519100
	UK	29	12386	94598	186706	3148138
	GR1	25	15900	102200	128400	5395400
	GR2	25 (winter: 6, summer: 19)	4700 (winter) 100 (summer)	333500 (winter) 111800 (summer)	366414 (winter) 184919 (summer)	6493000 (winter) 3921700 (summer)
Particle count (>2.5 µm), (particles/cubic foot of air)						
	NL	52	0	6100	17900	6149700
	UK	29	234.5	6710	33500	469193
	GR1	25	ND	5600	7900	627400
	GR2	25 (winter: 6, summer: 19)	ND (winter) ND (summer)	6400 (winter) 6400 (summer)	13190 (winter) 9732 (summer)	3554400 (winter) 529200 (summer)
Particle mass PM2.5 (µg m^{-3})*						
	NL	52	0.66	4.2	7.9	939
	UK**	29	2.8	8.0	8.9	21
	GR1	25	1.3	5.1	6.25	682
	GR2	25 (winter: 6, summer: 19)	0.8 (winter) 0.7 (summer)	16.3 (winter) 5.5 (summer)	18 (winter) 8.9 (summer)	932 (winter) 405 (summer)

*Using Semple et al. 2015 (Semple et al., 2015) equation, PM2.5 = 0.65 + 4.16 × 10−5 × [PNC] + 1.57 × 10−11 × [PNC]2 (Indoor)

**Values shown are based on household means

Comparison of the summary statistics indicates that differences in climate, indoor sources, and building characteristics likely explain the differences in indoor environmental quality parameters. In the Netherlands and the UK, no smokers were reported in the homes, and fireplaces were not used even in the winter. On the other hand, some of the homes in Greece included smokers and use of fireplaces.

3.2 Additional country-specific results

3.2.1 Netherlands

Conversion of the Dylos data

1. Fitting a calibration curve in residences

   In total PNC data were obtained with the Dylos (1 size bin in PM2.5 range) and the APS (22 size bins in the PM2.5 range) for 9 days in 3 Dutch homes. Figure 12 shows the Dylos counts on the x-axis versus the calculated mass based on the APS on the y-axis for all data points. The red line depicts the fitted curve based on data collected by these two instruments. The green and blue lines are the fitted curves as published by Semple and Dacunto, respectively.

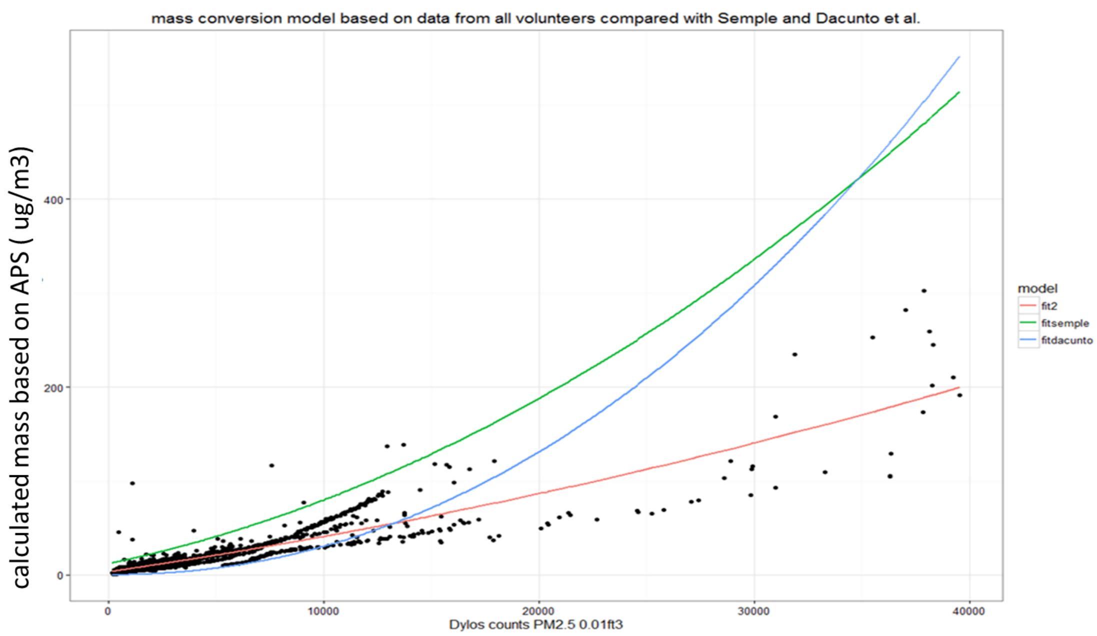


Figure 12: Data from Dylos and APS in the Netherlands fit with three different models

2. External validation of the methodology

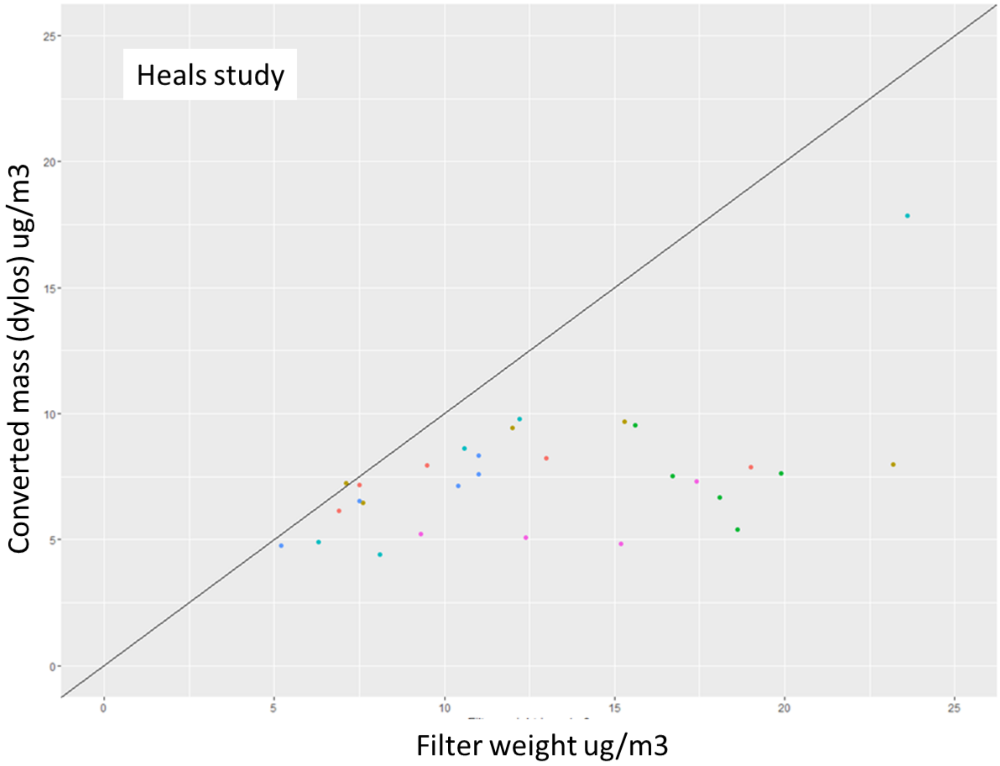


Figure 13: Dylos data converted using APS data vs. 24 h integrated impactor samples for PM2.5

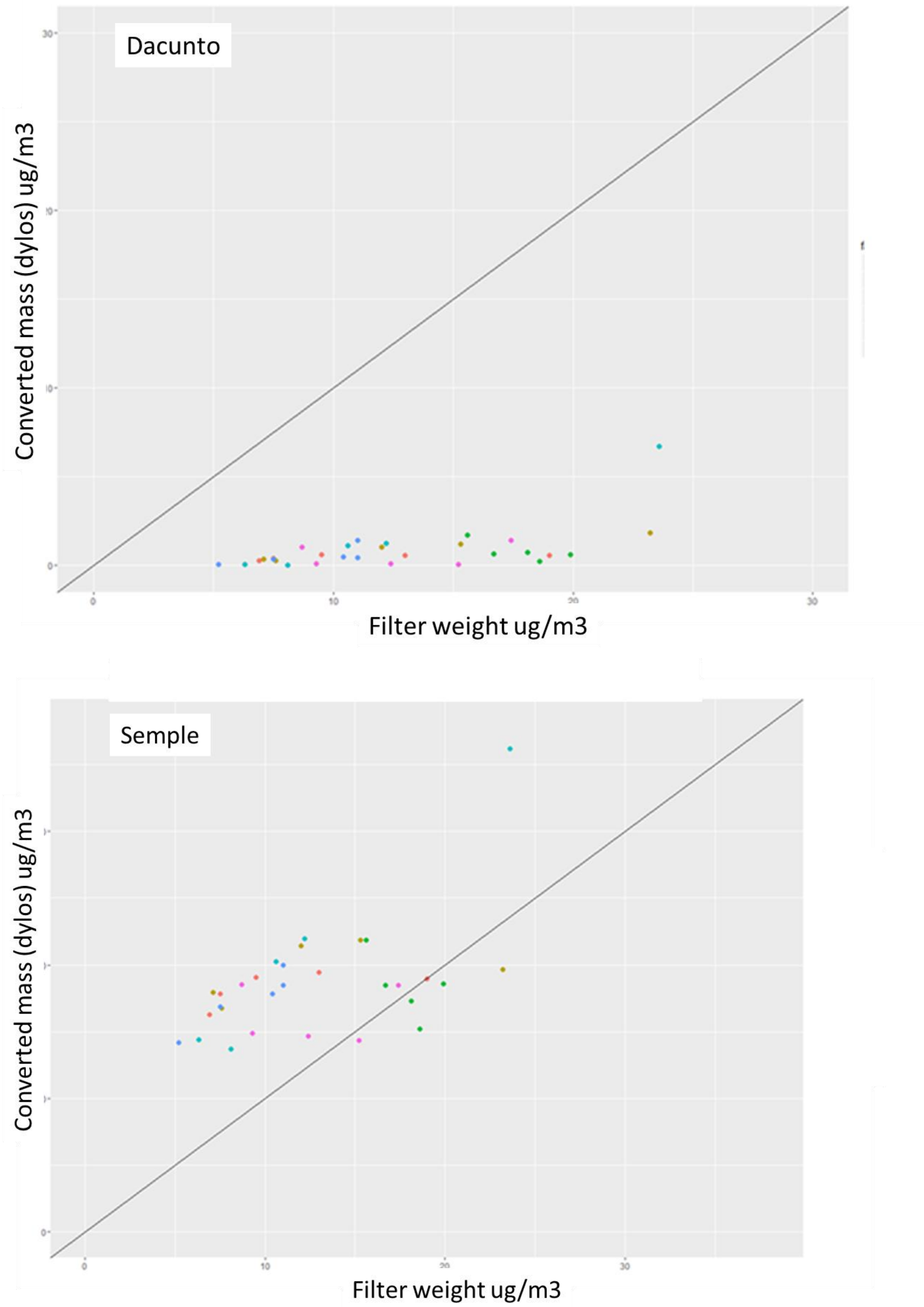


Figure 14: Comparison of 24-h averaged filter mass concentrations of PM2.5 collected gravimetrically compared to mass concentrations converted from Dylos particle number counts based on a) Semple, and b) Dacunto

Figure 13 and Figure 14 show plots comparing Dylos particle count data converted to mass concentration using different methods versus gravimentric samples collected over 24 hours (in 5 Dutch homes). All methods show considerable variation in the converted mass for the same gravimetrical result (up to a factor 4). This is likely explained by the fact that many sources of PM2.5 may exist within a home, with differences in particle composition and particle density. The fit curve obtained in this study seems to slightly underestimate the PM mass levels, the fit curve obtained by Semple seems to slightly overestimate and the fit curve obtained by Dacunto greatly underestimate the mass. It should be noted that the majority of the PNC counts obtained in this study population were below 10000 particles/ 0.01 ft^2. The concordance correlation coefficients were weak to moderate (0.21 for the current study, 0.28 for Semple and 0.04 for Dacunto). These concordance cofficients may be slightly improved by calibrating the APS conversion.

3.2.2 Greece

Preliminary data of additional monitors are listed below. These will be compared to the sensors used in the study.

AQ monitor - Athens

	Number Subjects	Minimum	Median	Mean	Maximum
Temperature (◦ C)	13	15.2	27.1	26.2	33.7
Relative Humidity (%)	13	19.4	45.8	47.3	71.6
CO (ppm)	13	ND	0.20	0.60	14.3
CO_2 (ppm)	13	373	528	655	4893
NO (ppm)*	13	ND	ND	ND	ND
NO_2 (ppm)*	13	ND	ND	ND	ND
TVOCs (ppb)	13	ND	50	144	6750

*ND: Not Detected due to very low limits of NO_x mass

AQ monitor – Thessaloniki (3 households during winter time – December 2015, January 2016)

	Number Subjects	Minimum	Median	Mean	Maximum
Temperature (◦ C)	3	12	16.9	17.7	26.2
Relative Humidity (%)	3	31.9	53.4	49.8	60
CO (ppm)	3	ND	1.70	1.70	4.60
CO_2 (ppm)	3	415	739	824	2199
NO (ppm)	3	ND	ND	ND	ND
NO_2 (ppm)*	3	ND	0.10	0.095	0.20
TVOCs (ppb)	3	ND	255	277	1614

*ND: Not Detected due to very low limits of NOx in residences and the low sensitivity of this monitor to these pollutants.

Grimm -Athens

	Number Subjects	Minimum	Median	Mean	Maximum
PM_1 (μg/m^3)	8	0.22	8.20	8.40	212
$PM_{2.5}$ (μg/m^3)	8	0.36	10.2	11.2	371
PM_{10} (μg/m^3)	8	0.49	18.4	17.9	658

Aerocet - Athens

	Number Subjects	Minimum	Median	Mean	Maximum
PM_1 (μg/m3)	9	0.18	1.0	1.2	18.4
$PM_{2.5}$ (μg/m3)	9	1.30	8.0	8.4	701
PM_{10} (μg/m3)	9	2.40	23.1	23.6	1634

Aerocet – Thessaloniki

	Number Subjects	Minimum	Median	Mean	Maximum
PM_1 (particles/m^3)	4	153655	1075591	1674985	28681384
$PM_{2.5}$ (particles/m^3)	4	ND	12009	37297	7316142
PM_{10} (particles/m^3)	4	ND	1059	6587	1913458

Aeroqual O_3

	Number Subjects	Minimum	Median	Mean	Maximum
O_3 (ppb)	13 (Athens)	ND	10.0	11.5	50
	6 (Thessaloniki)	ND	7.0	7.0	34

Aeroqual NO_2

	Number Subjects	Minimum	Median	Mean	Maximum
NO_2 (ppm)	13 (Athens)	ND	0.023	0.025	0.090
	2 (Thessaloniki)	ND	0.012	0.014	0.049

3.2.3 United Kingdom

Of the 10 homes that also had 24 hour integrated gravimetric samples taken, 4 homes had values above the detection limit (5 μg/m^3). Substituting the LOD/sqrt(2) for the values below the detection limit for which a positive value was not available after blank correction, the mean was 11 μg/m^3 (sd = 10 μg/m^3).

3.3 Fieldwork experience summary

Table 10: Summary of experiences with data collection devices in each country. Green indicates the device was well received by both participants and researchers and recommended as a potential tool for future use. Yellow indicates mixed reviews. Red indicates generally not liked by participants and researchers.

Device	Netherlands	UK	Greece	Comments
Sensor based apps ("low-cost" commercially available technologies)				
Fitbit				UK, GR: generally liked, but sometimes forgotten or uncomfortable during sleep; sometimes errors in activity type NL: The Fitbit was considered user friendly by most participants in this study. Participants found the steps taken, calories burned and sleep log very insightful and interesting.
MOVES app (on phone)				UK: battery drain problems; sometimes says there is a GPS error; not always carried GR: In the case of Greece a separate smartphone was used, therefore due to battery drain problems, participants had to charge this additional device at a daily basis; location accuracy was low when signal strength was weak NL: MOVES was diversely rated by participants. Participants who carried their phones all the time were generally more positive about this application than participants who did not constantly wear their phone.

Device	Netherlands	UK	Greece	Comments
Netatmo				UK,GR: can take several tries to set up; need good wifi signal NL: Participants of the study rated the device very positive. Many mentioned that the device and application is very user friendly and that the data is insightful.
Widenoise Plus app				UK, GR: people forget; not user friendly, one account per phone only – fieldwork phone users could access NL: Satisfaction on Widenoise Plus was relatively low therefore stopped using. The application is not considered user friendly by most of the participants.
Dylos DC1700				UK: noise was noticeable for some NL: The Dylos is considered user friendly by the participants because they do not have to operate the device. About half of the participants were bothered by the sound of the Dylos during the study.

Device	Netherlands	UK	Greece	Comments
Fatsecret app				UK: difficult to use with self-cooked food; takes a lot of time; can't have 2 accounts on one device; don't like name GR: Greek participants did not use the application, therefore a separate food diary was used NL: The Fatsecret application has been diversely rated by participants. Some participants found the use of a food diary insightful for their calorie intake (together with the calories burned from the Fitbit), and user friendly to use (barcode scanner), and would continue to use this application after the study. Other participants were less positive about the application. Main reasons were, very time consuming to keep track of food consumption for both the guardian and the child, restaurant food was hard to find in the application, not very user friendly, and lastly, for some participants the food diary affected the food intake during the week because the current calorie intake is visible for the participants.

Device	Netherlands	UK	Greece	Comments
Redlaser app; phone camera				UK: app didn't work well; taking photos was better but sometimes people forgot so researchers took photos during second visit GR: Consumer products were not recognized by the application, therefore a consumer product paper log was used instead. NL: Redlaser was positively rated by participants of this study for user friendliness, since the application was rather easy to use. However, participants found the application not very insightful since the application did not recognize most of the barcodes scanned.
Non-sensor samples				
Dust from vacuum cleaner				UK: no complaints GR: Greek participants seemed hesitant to share a sample of their vacuum bag with the research team. NL: Most participants were ok with collecting dust from the vacuum dust cleaning bag. However, collecting the entire bag was not agreed by most of the participants.
Dust settled onto electrostatic sheet				UK: no complaints NL: The passive sampler for dust was rated generally high by participants because they did not have to do anything with it.

Device	Netherlands	UK	Greece	Comments
Questionnaires*				
Building/area characteristics				UK: Some questions not relevant; some questions need better specification NL: In general, participants commented that the questionnaire was too long and on some parts unclear. Specifically, multiple participants found that question 12A from the observational questionnaire was unclear.
Indoor home activities				UK: filled in with varying levels of detail. May need better instructions on what to log
Socioeconomic status				UK, GR: people found it too long NL: In general, participants commented that the questionnaire was too long.
Noise (2 questionnaires)				UK, GR: Confusion because of similarity of questions NL: No comments
Electromagnetic fields				UK: most questions were found to be not applicable
User experience				UK: valuable for feedback GR: questionnaire was not used. A personal interview took place instead in order to collect feedback from every household.

3.4 Recommendations

The HEALS pilot study evaluated the use of various sensors for characterizing the external exposome. The sensors monitored the internal home environment and the locations and activities of the subjects, in this case a child and their guardian/caretaker. The sensor data was supplemented by dust samples and, will be, in future analyses, integrated by other sources of environmental data to develop models of individuals' exposure to multiple aspects of the environment. These can then be used to develop external exposome profiles for individuals, which can be linked to internal exposome (biomarker) profiles; in turn the latter can be linked to health outcomes.

We found that the Fitbit, Netatmo, MOVES, and Dylos were most acceptable to participants. These were also the devices that were most easily accessible for the researchers, with the Fitbit, Netatmo, and MOVES having APIs allowing researcher access to more detailed information in some cases, and also to downloading the data without needing to ask the participant to do anything. Using these devices, we can already develop profiles for participants about their general indoor climate, physical activity, and we have data on their daily trajectories that can be used, with additional datasets, to model personal exposures to various environmental hazards and benefits.

Participants did not like apps/devices which required them to remember to take action in terms of recording activities, spend a lot of active time doing, or which were not easy to do, such as the Fatsecret diet app and Widenoise + app. Also, given that the Fatsecret app was difficult to use for self-prepared meals, and was primarily a weight reduction tool, rather than a dietary exposure tool, the data collected may lack accuracy. In the future, dietary assessment may be better done using a periodic food frequency questionnaire or a more passive method of daily food recording, such as photos. The latter, however, has the disadvantage of potentially requiring a greater amount of processing by research staff, and, to date, there has not yet been a satisfactory photo tool devised for dietary assessment.

As mobile sensors and apps are not able to cover the universe of environmental exposures, these data must be supplemented. While often public offices collect data on issues such as air and water quality, and other environmental aspects, indoor environmental quality is still not regularly monitored. As homes and offices are private spaces, permission must be granted to do monitoring in these areas. Currently, sensors are not able to successfully measure many contaminants in environmental media. Even air quality sensors do not cover all types of air pollutants. Therefore, additional samples and laboratory analyses must be done to assess exposures to a wide range of contaminants. Passive sampling methods are most acceptable to participants.

Questionnaires are also needed to supplement sensor and sample collected data. These provide data on exposures that are not easily measured, and on factors that influence exposures, such as cleaning frequency, socioeconomic status, and occupation. However, questionnaires may be quite lengthy and participants may not wish to respond to them too often. Additionally, we found that many participants did not feel comfortable answering some of the questions, especially on the SES questionnaire.

3.5 Next steps

This document has described preliminary results from the HEALS sensors pilot. Recommendations for sensors as part of an external exposome sampling strategy have been made in this document. Analyses of the data collected by the pilot are ongoing with preliminary results shown here. The next part of this deliverable, D9.2B will discuss modelling methods to estimate exposures over the life course using the type of external exposome data that can be collected using methods developed here, and demonstrate these methods retrospectively, although these methods can also apply to prospective studies. These are briefly described here and will be described in more depth in D9.2B.

3.5.1 Agent based modelling

A major objective of HEALS is to integrate existing datasets and to fill data gaps in order to unravel the external exposome of individuals and population subgroups to multiple stressors via different pathways. Innovations in sensor technology create possibilities to collect environmental data at

unprecedented depth and breadth. With the advent of GIS, GPS to track individuals, and personal environmental monitoring, undertaking such analyses throughout an individual's routine, or even lifetime, is being carried out in WP9 as the previous sections have discussed. The use of Agent-Based Models (ABMs) enables us to better understand the behaviour of individuals and populations in social and evolutionary settings. Thus, the HEALS thesis is that ABMs will allow us to 'fill-in' the gaps in the exposome currently not available from real-world monitoring and sensor data. Moreover data on lifestyle/behaviour patterns (e.g. time-activity patterns for various activities per gender and age group) and SES data (e.g. information on educational level, income, occupational status) derived from EU scale or regional studies and surveys are also implemented into the model. Survey outputs are associated with human agent behavioural rules, with the aim to model representative to real world conditions.

Currently in HEALS the focus of ABM has been on population wide assessments where we are able to model individuals in a population with similar socio-economic characteristics and estimate their exposure (see D10.2 for further information). In doing so we are able to fill in gaps for members of society we have limited information on. It is envisaged the ABM can be applied to the HEALS cohort as well as the population wide study, and fill in gaps through an individual's life course, for example, from infancy to adolescence. To do this a retrospective ABM will be developed to fill in gaps of data collection. Retrospective agent based modelling has only just begun to emerge in social science (Hammond, 2015) and less so in epidemiological studies. The retrospective ABM will provide insight into the complex and dynamic mechanisms that exit when estimating the exposome that may not be observable due to gaps in data collection. In the case of HEALS, data will not exist for certain periods of the individuals life and ABM can help with causal inference methods to estimate an individual's exposome. One consideration is that much quantitative data, including most surveys, come from measurements made at a single moment in time (Gilbert, 2004). However, individuals change through their life course but it is difficult to monitor to them at every critical period. Therefore, in order to have a useful retrospective model it is important to ask retrospective questions about the individuals past during data collection. Limitations such as these are fairly well known and the advantage of an ABM is that we are able to simulate and fill gaps based on behavioral theory and existing data.

3.5.2 Life exposure trajectories for prospective and retrospective exposure characterization

By assessing determinants of life trajectories we aim to estimate past exposure both retrospectively and future exposure prospectively for individuals, including for vulnerable groups. The model will be defined in a probabilistic manner to allow for incorporation of uncertainty during all stages of the assessment. A prototype implementation of the concept is presented in this section.

In social sciences, sequence analysis is a key approach to study life trajectories (Studer & Ritschard (2016), Widmer & Ritschard (2009)). It allows to identify trajectory patterns that account for all states of interest and, more importantly, transitions between states. For the first time we will use this analysis approach in the field of exposure science to develop a probabilistic life exposure trajectory model that links life trajectories with time-activity patterns and an activity-exposure matrix to establish a life exposure trajectory model.

This modelling approach towards prospective and retrospective exposure characterization using estimates of life course trajectories will use information collected at individual or group level to

reconstruct past and estimate future life trajectories. We developed this approach as part of a 3-tier methodology in which

- Level 1: Estimate life trajectories of main activities (years in a lifetime)
- Level 2: Estimate time-activity within the year (minutes in a day)
- Level 3: Estimate exposure at location/activity level

For the Level 1 part of the methodology, we use data of the European Union Statistics on Income and Living Conditions (EU-SILC) longitudinal studies in which 4-year surveys were conducted (see HEALS Deliverable D11.1 for a description). Time-activity patterns (i.e. episode files of individuals) as the one in the Multinational Time Use Survey (MTUS) (see HEALS D11.1) are used in the Level 2 part of the methodology. The exposure estimation follows along the approach sketched in D11.1 utilizing the environmental data and exposure data from Stream 3 data synthesis efforts.

In D9.2B, we will focus on the first level of this overall approach, i.e. the life trajectories. Based on an individual's current stage in life and several life-course characterizing factors like age, gender and current educational and/or current employment situation we estimate potential future life-course trajectories along with their probability of occurrence. For groups of individuals, we estimate the potential future life trajectories in a very similar way and, if unknown, estimate probabilities of past trajectories that may have happened.

The backbone of the estimation approach is to analyze collections of recorded life trajectories of individuals retrospectively and regress certain socio-economic factors with the aim of transferring the information and predict future developments in life and estimate past trajectories in case they are not known.

4 Conclusions

HEALS WP9 has investigated methods for prospective study of the external exposome using sensors and smartphone technologies. The sensors methods allows for collection of data on subjects' location and activity data, and exposure information regarding their home environment. The sensor and smartphone data can be supplemented by questionnaires and additional environmental samples and data on parameters from public datasets (see HEALS Workpackage 8).

Generally, the most successful data collection methodologies were ones where participants did not have to go out of their way to use, and which provided information that they found interesting while using the method. These also translate into methods that are well designed for both participant and researcher use. Such methods are likely to be more successful for long-term data collection. Sensors, however, cannot cover a wide range of exposures. It is recommended that physical activity, location tracking, and in-home environmental monitors can be used relatively unobtrusively and with high participant acceptance. Other exposure measurements place a relatively high burden on participants, for example personal noise dose measurement, consumer product use and diet data recording. Questionnaires are also time consuming. Further research is needed into reducing participant burden when using these more intensive methods of data collection.

Modelling methods can be used to estimate the external exposome retrospectively and prospectively, supplementing primary data collection to "fill in the gaps" where data is not available, and to estimate life course trajectories. These methods will compose the second part of this deliverable, D9.2B.

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