EXPOSURE ASSESSMENT PROTOCOLS

Deliverable D2.1

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Contents

1. Introduction

The aim of this document is to describe the protocols for Task 2.3.2 ‘Personal monitoring data in cohort and intervention study subjects’ and Task 2.4 ‘Assessing the external exposome’.

Using wearables and indoor monitors, **Task 2.3.2 ‘Personal monitoring data in cohort and intervention study subjects’** will obtain personal monitoring data on physical activity, air pollution, and sleep **in the new HELIX subcohort follow-up**, that include a subsample of children from six cohorts, namely BiB, EDEN, INMA, KANC, MoBa and RHEA (**N~1100).** These will provide objective measures for comparison with questionnaires and geospatial models and improved exposure estimates for these exposures.

Task 2.4 ‘Assessing the external exposome’ will provide integrated and harmonised exposure indices for the external exposome **in all 15 ATHLETE cohorts**. Exposures covered by the external exposome include outdoor air pollution, road traffic noise, meteorological factors, ultraviolet, light, built environment, natural spaces, traffic and transport, social deprivation and food environment.

2. Personal monitoring in cohort and intervention study subjects (Task 2.3.2)

In Task 2.3.2, we will obtain **personal monitoring data** on **physical activity and sedentary behaviour** (GeneActiv, Actigraph, and EXPOApp3), **air pollution** (nitrogen dioxide, NO2, passive diffusion tubes, Gradko), **sleep** (GeneActiv), and **mobility** (EXPOApp3) using wearables, smartphones and indoor monitors during a one-week period between the Visit 1 (clinical examination) and Visit 2 (blood drawn) of the new HELIX subcohort follow-up (N~1100) (N~180 in each subcohort) (Jan-Dec 2021), as summarized in Table 1. These will provide objective measures for comparison with questionnaires and geospatial models and improved exposure estimates for these exposures. After evaluating the LANCube included in the proposal for light monitoring, and performing an internal validation, we decided to not include them in the personal monitoring protocol because they are too bulky.

Table 1 List of exposure variables

Exposure group	Exposure variables	Methods for new data generation	New data to be generated
Personal monitoring			
Personal air pollution	NO2	Diffusion tubes	HELIX subcohort follow-up
Physical activity	Physical activity duration and intensity	GeneActiv (wrist worn), Actigraph (hip worn), EXPOApp3	HELIX subcohort follow-up (Actigraph in a subsample of the children for validation of GeneActiv)
Sleep	Sleep duration	GeneActiv (wristwatch)	HELIX subcohort follow up
Mobility	Time spent in different environments	EXPOApp3	HELIX subcohort follow-up

2.1. Personal air pollution

The Standard Operational Procedure (SOs) for NO2 personal monitoring with palmes passive diffusion tubes is detailed in Annex 1.

2.2. Physical activity

Physical activity, including step count, number of physical activity bouts, caloric expenditure (via metabolic equivalent of task, METs) will be measured using two types of actigraphs (GeneActiv, a wrist-worn accelerometer, and Actigraph, a hip-worn-accelerometer) and the EXPOApp3 installed on smartphones (for the latter see Deliverable D2.2). GeneActiv will be used in the entire HELIX subcohort, since the use of a wrist-worn device has been demonstrated to be more acceptable in adolescents[1], and will also be used to monitor sedentary behaviour and sleep. The hip worn Actigraph will be used in a subsample for internal validation of the GeneActiv data.

The SOPs for GeneActiv and Actigraph are in Annexes 2 and 3 respectively.

2.3. Sleep

Sleep duration and sleep latency will be assessed using the GeneActiv wrist-worn accelerometer already in use for physical activity measurement (see section 2.2).

2.4. Mobility

EXPOApp3 is described in Deliverable D2.2 (month 6).

[1] Joseph J. Scott et al., 'Comparability and Feasibility of Wrist- and Hip-Worn Accelerometers in Free-Living Adolescents', *Journal of Science and Medicine in Sport* 20, no. 12 (1 December 2017): 1101–6, https://doi.org/10.1016/j.jsams.2017.04.017.

3. Assessing the external exposome (Task 2.4)

The urban environment has been shown to affect health in children in some specific areas, but a more consistent approach across Europe is needed to develop community level intervention and prevention strategies.

As part of the HELIX and LifeCycle projects we built a platform for geospatial modelling of the external and urban exposome in birth cohorts. Following these existing protocols, exposures (outdoor air pollution, road traffic noise, climatic factors, ultraviolet, light, built environment, natural spaces, traffic and transport, social deprivation and food environment) will be estimated using geospatial models, monitoring stations, satellite data and land use databases, and assigned to study participants according to their geocoded home and school addresses using GIS platforms (described in detail by Robinson et al. (2018)[2], Nieuwenhuijsen et al 2019[3], Tamayo et al 2019[4]).

Task 2.4 will provide integrated and harmonised exposure indices for the external exposome and ambient chemical and physical exposures following methods detailed in this protocol in all 15 ATHLETE cohorts. Exposures covered are summarized in Table 2 and include outdoor air pollution, road traffic noise, climatic factors, ultraviolet, light, built environment, natural spaces, traffic and transport, social deprivation and food environment.

This task will leverage work of previous projects (HELIX and LifeCycle) on the urban exposome by including: i) new follow-ups (preconception and last follow up) in those cohorts for which GIS work has already been done as part of HELIX and LifeCycle; ii) new cohorts (BiSC, ENVIRONAGE, Gen R Next, PELAGIE, SEPAGES); iii) and new indices of specific interest such as food environment, and light at night exposure using satellite images (summarized in Table 2). The planned streetscape work using Google street view is not possible at the moment due to a recent change in the Google licence terms that do not allow download of Street view imagery for use outside the Google Services, but we are talking to the EXPANSE project to get access to their Google street view data. Data will be processed in a GIS environment to link spatial data to residential and school addresses.

QGIS software[5] will be used to trace the usual commuting routes of participants in the new HELIX follow-up directly on the computer. Data on location and mobility collected in Task 2.3.1 (see Deliverable 2.2 'ExpoApp') will be used to characterise where the participants spend their time and where they are exposed, in real-time. This information will then be integrated with the external exposome estimates to provide exposure estimates at different locations and for different micro-environments (e.g., home, school, commuting exposures).

A total of 75,000 mother-child pairs from 15 cohorts from ten European countries are available for generating the integrated harmonised exposure indices for stressors in the urban environment the

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[2] Léa Maitre et al., 'Human Early Life Exposome (HELIX) Study: A European Population-Based Exposome Cohort', *BMJ Open* 8, no. 9 (1 September 2018): e021311, https://doi.org/10.1136/bmjopen-2017-021311.
[3] Mark J. Nieuwenhuijsen et al., 'Influence of the Urban Exposome on Birth Weight', *Environmental Health Perspectives* 127, no. 4 (2019): 47007, https://doi.org/10.1289/EHP3971.
[4] Ibon Tamayo-Uria et al., 'The Early-Life Exposome: Description and Patterns in Six European Countries', *Environment International* 123 (1 February 2019): 189–200, https://doi.org/10.1016/j.envint.2018.11.067.
[5] 'QGIS Development Team. QGIS Geographic Information System. Open Source Geospatial Foundation Project.', 2020, http://www.qgis.org/en/site/.

exposure in this task (Table 3). The final N for each exposure will vary depending on the availability of GIS data in each cohort.

Table 2 List of exposure variables

Exposure group	Exposure variables	Methods for new data generation	New data to be generated
Outdoor exposome			
Outdoor air pollution	NO_2, $PM_{2.5}$, PM_{10}, $PM_{2.5abs}$ Composition	ESCAPE LUR models and ELAPSE air pollution models	New cohorts and new follow-ups
Road traffic noise	Noise levels	Regulatory noise maps	New cohorts and new follow-ups
Climatic factors	Temperature, relative humidity, pressure	Daily average from city monitoring stations	
Ultraviolet (UV)	Ambient UV radiation levels	Remote sensing	
Light	Night-time light exposure	Remote-sensing	
Commuting routes	Commuting routes & modes	qGIS	HELIX subcohort follow up
Built environment	Population and building density, street connectivity, facility density, land use, walkability	Land cover/use maps	New cohorts and new follow-ups
Natural spaces including green space	Residential surrounding greenness, distance to nearest green and blue spaces	Remote sensing and land cover/use maps	
Traffic and transport	Traffic load, distance to roads, public transport network	Land use maps	
Social deprivation	Area level indicators	To be generated	
Food environment	Fast food restaurants, healthy food places	Facilities maps	

Table 3 ATHLETE cohorts involved in Task 2.4

Cohort	Years birth	Country	Cities	N at birth	Preg	0-6y	6-12y	12-18y
HELIX Subcohort*	2003-2009	Bradford (UK), Poitier (FR), Sabadell (ES),Kaunas (LT), Oslo (NO), Heraklion (GR)		1,300				
BiB	2007-2010	UK	Bradford	13,858				
BISC	2018-2020	ES	Barcelona	1,200				
DNBC	1996-2003	DK	Copenhagen greater area	17,500				
EDEN	2003-2006	FR	Restricted to Nancy, Poitier	1,900				
GenR	2004-2006	NL	Rotterdam	7,000				
GenR Next	2017-2020	NL	Rotterdam	2,000				
INMA	2003-2008	ES	Restricted to Gipuzkoa, Sabadell, Valencia	2,060				
MoBa	1999-2008	NO	Restricted to Oslo region	11,090				
NINFEA	2005-2016	IT	Restricted to Florence, Rome, Turin	3,774				
RHEA	2007-2008	GR	Heraklion	1,500				
KANC	2007-2008	LT	Kaunas	4,100				
Piccolipiù	2011-2015	IT	Restricted to Florence, Rome, Turin	1,836				
PELAGIE	2003-2006	FR		3,400				
SEPAGES	2015-2018	FR		484				
ENVIRONAGE	2010-2019	BE		1,900				
TOTAL				74,902				

BLUE, exposure estimates already available; ORANGE, exposure estimates to be calculated in ATHLETE.
* the HELIX subcohort include a subsample of BiB (205), EDEN (198), INMA (223), KANC (204), MoBa (272) and RHEA (199).
BE, Belgium; DK, Denmark; ES, Spain; FR, France; GR, Greece; IT, Italy; LT, Lithuania; NL, The Netherlands; NO, Norway; UK, United Kingdom.

3.1. Exposure periods/time points to be generated

In terms of exposure periods/time points to be calculated, in this task we will extend the work done in LifeCycle by adding the preconception period and exposure periods/time points up to the the last available follow up in the cohorts involved in that project, i.e. HELIX subcohort, BiB, DNBC, EDEN, Gen R, INMA, MoBa-Oslo, NINFEA, RHEA, KANC, Piccolipiù. Moreover, for those cohorts not involved in LifeCycle, we will calculate all exposures periods/time points from pre-conception until last available follow up, if not already calculated by the cohort itself.

For those variables with daily temporal resolution (i.e. outdoor air pollution, climatic factors and UV radiation), the following exposure periods will be created (where not already calculated): pre-conception, trimesters, entire pregnancy, one year averages starting with date of birth up to last available follow up (using the last entire year including the date of follow up) (e.g. for a child born 12 May 2000 for which the last visit took place on 30 Sep 2010, the last exposure window that will be calculated will be 12 May 2010 – 11 May 2011) (this will allow researcher to build their own averages when needed).

For those variables without daily temporal resolution (i.e. road traffic noise, light at night, built environment, natural spaces, traffic and transport, social deprivation and food environment), the following exposure time points will be made available (if not already calculated): pre-conception, pregnancy, at birth, 1 point at each year (1, 2, …, x) up to the last available follow up (birthday after follow up).

For those cohorts with complete address history, exposure will be assigned at the exact geocode for each period/time point. In the case complete address history information is not available, we will assign the moving date in the middle of the interval for those participants who moved between two follow up visits.

GIS work will be done at ISGlobal. For this, from the cohorts we will need to receive geocodes as coordinates or point GIS layers of the addresses and address history as complete as possible, including pre-conception, as well as GIS input data.

For the period from pre-conception and up to eighteen years of age, the residential geocodes of the address history of 75,000 mother-child pairs will be transferred from cohorts to a central database held at ISGLOBAL in Barcelona.

3.2. Outdoor air pollution

We will create exposure estimates to the following outdoor air pollutants: NO_X, NO_2, $PM_{2.5}$, PM_{10}, $PM_{2.5abs}$, PM_{coarse}, and particles components. The exposure assessment (including particles composition) will be based on the land use regression (LUR) modelling approach developed in the European Study of Cohorts for Air Pollution Effects (ESCAPE) framework, that included most of the cohorts participating to this subtask[6]. For those cohorts for which ESCAPE local models were not

[6] Rob Beelen et al., 'Mapping of Background Air Pollution at a Fine Spatial Scale across the European Union', *Science of The Total Environment* 407, no. 6 (1 March 2009): 1852–67, https://doi.org/10.1016/j.scitotenv.2008.11.048; Josef Cyrys et al., 'Variation of NO2 and NOx Concentrations between and within 36 European Study Areas: Results from the ESCAPE Study', *Atmospheric Environment* 62 (December 2012): 374–90, https://doi.org/10.1016/j.atmosenv.2012.07.080; Marloes Eeftens et al., 'Development of Land Use Regression Models for PM2.5, PM2.5 Absorbance, PM10 and PMcoarse in 20

available, models developed within the ELAPSE project will be used[7] (only available for NO_2 and $PM_{2.5}$). PM_{10} local dispersion models[8] will be used for EDEN for the pregnancy period.

To obtain estimates for the relevant exposure period within ATHLETE, temporal adjustment will be conducted using background routine monitoring stations. Temporally adjusted exposure levels to each pollutant will be estimated for each study participant by combining the LUR spatial estimates of pollutants for their geocode with a temporal adjusting factor obtained from the routine monitoring data, following ESCAPE guidelines[9]. Specifically, it will be used the ratio of the concentration of the routine monitor of each day of the study period and the annual average during 2009 (year of sampling campaign) or 2010 (year of ELAPSE air pollution grid maps) as the adjustment factor for that day. When data on a specific pollutant is not available from the routine network we will do a back-extrapolation based on available pollutants as follow: we will use daily PM_{10} to adjust NO_2 and NO_x; NO_2 or PM_{10} factors to adjust $PM_{2.5}$; NO_2 to adjust PM_{10}; daily NO_x to adjust $PM_{2.5abs}$. Data on background NO_2, NO_x, PM_{10}, and $PM_{2.5}$ (the latter if available) concentrations will be obtained from routine background stations active during whole study period.

3.3. Road traffic noise

The noise exposure assessment will be based on existing European road traffic noise maps, which were generated under EC Directive 2002/49/EC (Assessment and Management of Environmental Noise) in the framework of the European Noise Directive (END), except for RHEA. A new noise map was developed by ISGlobal for RHEA making use of data generated in a traffic monitoring campaign done as part of the EXPOsOMICS project. The primary noise indicators are the Lden and the Lnight. Lden is the long-term average indicator designed to assess annoyance and defined by the END. It refers to an annual average of day, evening and night period of exposure. Lnight is the long-term average indicator designed to assess sleep disturbance and defined by the END. It refers to an annual average of night period of exposure.

Noise values were obtained depending on the noise layer type ("line", "polygon" or "raster"):

European Study Areas; Results of the ESCAPE Project', *Environmental Science & Technology* 46, no. 20 (16 October 2012): 11195–205, https://doi.org/10.1021/es301948k; Marloes Eeftens et al., 'Spatial Variation of PM2.5, PM10, PM2.5 Absorbance and PMcoarse Concentrations between and within 20 European Study Areas and the Relationship with NO2 – Results of the ESCAPE Project', *Atmospheric Environment* 62 (December 2012): 303–17, https://doi.org/10.1016/j.atmosenv.2012.08.038; Rob Beelen et al., 'Development of NO2 and NOx Land Use Regression Models for Estimating Air Pollution Exposure in 36 Study Areas in Europe – The ESCAPE Project', *Atmospheric Environment* 72 (June 2013): 10–23, https://doi.org/10.1016/j.atmosenv.2013.02.037; Kees de Hoogh et al., 'Development of Land Use Regression Models for Particle Composition in Twenty Study Areas in Europe', *Environmental Science & Technology* 47, no. 11 (4 June 2013): 5778–86, https://doi.org/10.1021/es400156t.

[7] Kees de Hoogh et al., 'Spatial PM2.5, NO2, O3 and BC Models for Western Europe – Evaluation of Spatiotemporal Stability', *Environment International* 120 (1 November 2018): 81–92, https://doi.org/10.1016/j.envint.2018.07.036.

[8] Annisa Rahmalia et al., 'Pregnancy Exposure to Atmospheric Pollutants and Placental Weight: An Approach Relying on a Dispersion Model', *Environment International* 48 (1 November 2012): 47–55, https://doi.org/10.1016/j.envint.2012.06.013.

[9] Gerard Hoek et al., 'A Review of Land-Use Regression Models to Assess Spatial Variation of Outdoor Air Pollution', *Atmospheric Environment* 42, no. 33 (1 October 2008): 7561–78, https://doi.org/10.1016/j.atmosenv.2008.05.057.

- doing an intersection between noise map and geocodes, if noise layer type was “polygon” or “raster”;
- assigning noise value from closest street, if noise layer type was “line”.

For those cohorts with layer type “line” another variable was created, indicating the distance to the closest street.

3.4. Climatic factors

3.4.1. Temperature and humidity

Meteorological stations in the study area will be used to obtain data on temporal variability in temperature. Daily meteorological data from meteorological stations measurements will be obtained for all the study period (temperature and humidity). Atmospheric pressure comes from ESCAPE project and it is available only for pregnancy period.

3.4.2. Land surface temperature

Spatial assessment of annual average exposure to heat will be based on MODIS Land Surface Temperature and Emissivity (MOD11A2)[10]. The Land Surface Temperature (LST) and Emissivity daily data are retrieved at 1km pixels by the generalized split-window algorithm and at 6km grids by the day/night algorithm. In the split-window algorithm, emissivities in bands 31 and 32 are estimated from land cover types, atmospheric column water vapor and lower boundary air surface temperature are separated into tractable sub-ranges for optimal retrieval. In the day/night algorithm, daytime and nighttime LSTs and surface emissivities are retrieved from pairs of day and night MODIS observations in seven TIR bands. The MOD11A2 Version 6 product provides an average 8-day per-pixel Land Surface Temperature and Emissivity (LST&E) with a 1 kilometer (km) spatial resolution in a 1,200 by 1,200 km grid. Each pixel value in the MOD11A2 is a simple average of all the corresponding MOD11A1 LST pixels collected within that 8-day period. One imagery per month from MOD11A2 product will be selected to calculate annual averages.

3.5. Ultraviolet (UV)

The UV dose is the effective UV irradiance (given in kJ/m2) reaching the Earth's surface integrated over the day and taking into account the attenuation of the UV radiation due to clouds. UV dose is computed for three different action spectra, i.e. for three different health effects: erythema (sunburn) of the skin, vitamin-D production in the skin and DNA-damage in the skin.

Data on daily spatial distribution of the ambient Ultraviolet radiation (UVR) levels will be obtained from TEMIS project[11]. It provides maps of daily Erythemal UV dose, Vitamin-D UV dose and DNA-damage UV dose from UVR levels adjusted for cloud cover, stratospheric ozone and atmospheric

[10] Wan, Z., S. Hook, G. Hulley, ‘MOD11A2 MODIS/Terra Land Surface Temperature/Emissivity 8-Day L3 Global 1km SIN Grid V006’, *Distributed by NASA EOSDIS Land Processes DAAC*, 2015, https://doi.org/10.5067/MODIS/MOD11A2.006.

[11] ‘TEMIS -- UV Index and UV Dose: Data Product Description’, accessed 27 May 2020, http://www.temis.nl/uvradiation/product/.

particles with a spatial resolution of 0.25° × 0.25°. UV value was obtained overlapping between UV raster map and geocodes.

3.6. Night-time light exposure

Assessment of annual average exposure to night-time light exposure will be based on two sources depending on the cohort's temporal period.

For temporal periods before 2013, version 4 DMSP-OLS Nighttime Lights Time Series from the Earth Observations Group (EOG) at NOAA/NCEI[12] will be used. The files are cloud-free composites made using all the available archived DMSP-OLS smooth resolution data for calendar years. The products are 30 arc second grids (the 30 arc-second grid spacing equates to about 1 kilometer, although that number decreases in the East/West (longitudinal) direction as latitude increases).

For temporal periods after 2013, version 1 Visible Infrared Imaging Radiometer Suite (VIIRS) Day/Night Band (DNB) Nighttime Lights from the Earth Observations Group (EOG) at NOAA/NCEI[13] will be used. The products are produced in 15 arc-second geographic grids (~500 m). Temporal averaging is done on a monthly and annual basis. The version 1 series of monthly composites has not been filtered to screen out lights from aurora, fires, boats, and other temporal lights. However, the annual composites have layers with additional separation, removing temporal lights and background (non-light) values. So annual composites will be used.

3.7. Commuting routes

In ATHLETE, commuting routes will be collected in the participants to the HELIX follow up visit using the qGIS geocoding questionnaire. The complete Standard Operating Procedure (SOP) for the qGIS is detailed in Annex 4.

3.8. Built environment

3.8.1. Population Density

Population density is the number of inhabitant per square kilometre. The Global Human Settlement Layer (GHSL)[14], a project supported by European Commission, will be used to characterize the population density for all the cohorts. Population density values will be obtained doing an intersection between population density grid maps and geocodes.

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[12] DMSP data collected by the US Air Force Weather Agency., *Image and Data Processing by NOAA's National Geophysical Data Center.*, n.d., n.d.

[13] DMSP data collected by the US Air Force Weather Agency.

[14] 'European Commission, Joint Research Centre; Columbia University, Center for International Earth Science Information Network (2015): GHS Population Grid, Derived from GPW4, Multitemporal (1975, 1990, 2000, 2015). European Commission, Joint Research Centre (JRC) [Dataset] PID: Http://Data.Europa.Eu/89h/Jrc-Ghsl-Ghs_pop_gpw4_globe_r2015a', n.d.

3.8.2. Building Density

Building density is the sum of the built area divided by the buffer area. The European Settlement Map 2017 (ESM2p5m)[15] will be used to create building density variable. ESM2p5m is the latest release of the European Settlement Map (ESM) produced in the frame of the URBA project.

3.8.3. Street Connectivity

Street network from each study area will be obtained using NAVTEQ[16] or Open Street Maps[17]. Intersection density is defined as the number of intersections - that are not dead-ends – inside a buffer of 100 and 300 meters, divided by the area in square km of each buffer. A higher value indicates more intersections and a greater degree of connectivity enabling more direct travel between two points using existing streets and pathways.

3.8.4. Accessibility

Public transport network and stops will be obtained from local authorities of each study area and/or from Open Street Maps in those cases where local layers were not available.

Public transportation network density will be calculated as meters of public transport lines (only bus lines) inside each 100, 300 and 500 meters buffer, divided by the buffer area in square kilometres. Public transportation stop density will be calculated as the number of public transport stops (only bus stops) inside each 100, 300 and 500 meters buffer, divided by the buffer area in square kilometres.

3.8.5. Facilities

Facilities from each study area will be obtained using NAVTEQ or Open Street Maps. Facilities are all points of interest for pedestrians as part of their daily life activities, like restaurants, shops, medical centres, schools, libraries, etc. One hundred different subcategories of facilities are available in the NAVTEQ database, grouped in 17 categories. All of them will be included, except Border Crossings, Auto Services and Parking categories.

Two different indicators will be calculated: facility richness index and facility density index.

- Facility richness index: equals the number of different facility types present divided by the maximum potential number of facility types specified, in a buffer of 300 meters. Range: 0 ≤ FRI ≤ 1. A higher value indicates a more availability of different facility types.

Equation 1 Facility richness (FR)

$$FR = \frac{m}{m_{max}}$$

[15] 'Commission Regulation (EU) No 1089/2010 of 23 November 2010 Implementing Directive 2007/2/EC of the European Parliament and of the Council as Regards Interoperability of Spatial Data Sets and Services, Date of Publication: 2010-12-08', n.d.

[16] 'Navteq(a) Street Data (2012). Navteq Is Licensed Data under ArcGIS Software.', n.d.

[17] 'OpenStreetMap® Is Open Data, Licensed under the Open Data Commons Open Database License (ODbL) by the OpenStreetMap Foundation (OSMF).', OpenStreetMap, accessed 19 December 2016, https://www.openstreetmap.org/.

m = number of facilities types (classes) in the study area

- Facility density index: equals the number of facilities present divided by the area of the 300 meters buffer (number of facilities / km2). A higher value indicates a more availability of different facility types.

3.8.6. Land Use Mix

Land Use Mix corresponds to the diversity of land uses within a given area. Land Use Mix will be obtained through the Shannon’s Evenness Index, using Urban Atlas database. In case this layer is not available, local data or Corine Land Cover[18] will be used. Land use Shannon's Evenness Index is the degree of mixing of different types of land uses. A higher value indicates a more even distribution of land between the different types of land uses. Land Use Evenness Index equals minus the sum, across all land use types, of the proportional abundance of each land use type multiplied by that proportion, divided by the logarithm of the number of land use types, in a buffer of 300 meters. In other words, the observed Shannon's Diversity Index[19] divided by the maximum Shannon's Diversity Index for that number of land use types. One or two maps will be selected for each cohort/city to cover the entire study period, and assigned to time points of interest.

Equation 2 Land Use Shannon's Evenness Index (LUEI)

$$LUEI = \frac{-\sum_{i=1}^{m} \quad (Pi * ln\ Pi\ )}{ln\ m}$$

Pi = proportion of the area occupied by land use type (class) i.

m = number of land use types (classes) present in the study area

LUEI = Land Use Shannon’s Evenness Index

3.8.7. Main Land Use

Main land use gives the percentage of all types of land use within an area of a buffer of 300 meters for each geocode. Land use information will be obtained from the Urban Atlas database[20]. In case this layer is not available, local data will be used. One or two maps will be selected for each cohort/city to cover the entire study period, and assigned to time points of interest. The following main land use categories are going to be created, by grouping the land use categories available in the selected databases: “high density residential”, “low density residential”, “very low density residential”, “industrial, commercial, public, military and private units”, “transports”, “port areas”, “airport areas”, “other”, “urban green”, “agricultural green”, “natural green”, “water”.

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[18] *Corine Land Cover 2006 The European Topic Centre on Spatial Information and Analysis. (CLC2006), Vector Database (Version 12/2013)*, n.d., n.d., http://www.eea.europa.eu/data-and-maps/data/corine-land-cover-2006-raster-3#tab-gis-data.

[19] C. E. Shannon, ‘A Mathematical Theory of Communication’, *SIGMOBILE Mob. Comput. Commun. Rev.* 5, no. 1 (January 2001): 3–55, https://doi.org/10.1145/584091.584093.

[20] European Environment Agency, ‘Urban Atlas’, Data, 2010, http://www.eea.europa.eu/data-and-maps/data/urban-atlas.

Table 3 Urban atlas categories (year 2006 version)

vector data code	nomenclature	main land use category
11100	Continuous Urban Fabric (S.L. > 80%)	hdres
11210	Discontinuous Dense Urban Fabric (S.L. 50% - 80%)	ldres
11220	Discontinuous Medium Density Urban Fabric (S.L. 30% - 50%)	ldres
11230	Discontinuous Low Density Urban Fabric (S.L. 10% - 30%)	ldres
11240	Discontinuous Very Low Density Urban Fabric (S.L. < 10%)	vldres
11300	Isolated structures	vldres
12100	Industrial, commercial, public, military and private units	indtr
12200	Road and rail network and associated land	trans
12210	Fast transit roads and associated land	trans
12220	Other roads and associated land	trans
12230	Railways and associated land	trans
12300	Port areas	port
12400	Airports	airpt
13100	Mineral extraction and dump sites	other
13300	Construction sites	other
13400	Land without current use	other
14100	Green urban areas	urbgr
14200	Sports and leisure facilities	urbgr
20000	Agricultural areas, semi-natural areas and wetlands	agrgr
30000	Forests	natgr
50000	Water	water

Legend: hdres, high density residential; ldres, low density residential; vldres, very low density residential; indtr, industrial, commercial, public, military and private units; trans, transports; port, port areas; airpt, airport areas; agrgr, agricultural green; urb, green urban areas, sports and leisure facilities; natgr, natural green.

Table 4 Urban atlas categories (year 2012 version)

vector data code	nomenclature	main land use category
11100	Continuous Urban Fabric (S.L. > 80%)	hdres
11210	Discontinuous Dense Urban Fabric (S.L. 50% - 80%)	ldres
11220	Discontinuous Medium Density Urban Fabric (S.L. 30% - 50%)	ldres
11230	Discontinuous Low Density Urban Fabric (S.L. 10% - 30%)	ldres
11240	Discontinuous Very Low Density Urban Fabric (S.L. < 10%)	vldres
11300	Isolated structures	vldres
12100	Industrial, commercial, public, military and private units	indtr
12210	Fast transit roads and associated land	indtr
12220	Other roads and associated land	trans

12230	Railways and associated land	trans
12300	Port areas	port
12400	Airports	airpt
13100	Mineral extraction and dump sites	other
13300	Construction sites	other
13400	Land without current use	other
14100	Green urban areas	urbgr
14200	Sports and leisure facilities	urbgr
21000	Arable land (annual crops)	agrgr
22000	Permanent crops	agrgr
23000	Pastures	agrgr
24000	Complex and mixed cultivation	agrgr
25000	Orchards	agrgr
31000	Forests	natgr
32000	Herbaceous vegetation associations	natgr
33000	Open spaces with little or no vegetation	natgr
40000	Wetlands	agrgr
50000	Water	water

Legend: hdres, high density residential; ldres, low density residential; vldres, very low density residential; indtr, industrial, commercial, public, military and private units; trans, transports; port, port areas; airpt, airport; agrgr, agricultural green; urb, green urban areas, sports and leisure facilities; natgr, natural green.

Table 5 Kartverket categories (used for MoBa)

kartverket	main land use category
Farmland	agrgr
Densely populated area, desnely built-up area	hdres
Industrial area	indtr
Urban area	ldres
Open area	natgr
Vood, forest	natgr
Stone quarry	other
Gravesite, burial ground, burial site	urbgr
Athletic and sports ground, playing field	urbgr
Golf Course (or golf links)	urbgr
Alpine ski hill	urbgr
Park	urbgr
Surface of the sea (sea level)	water
River/Brook (small stream)	water
Bog, marsh	water

Lake	water

Legend: hdres, high density residential; ldres, low density residential; vldres, very low density residential; indtr, industrial, commercial, public, military and private units; trans, transports; port, port areas; airpt, airport; agrgr, agricultural green; urb, green urban areas, sports and leisure facilities; natgr, natural green.

Table 6 EUNIS categories (used for INMA Guipuzkoa)

eunis code	level	eunis name	main land use category
A	1	Marine habitats	water
B	1	Coastal habitats	natgr
C	1	Inland surface waters	water
D1	2	Raised and blanket bogs	water
D2	2	Valley mires, poor fens and transition mires	natgr
D3	2	Aapa, palsa and polygon mires	natgr
D4	2	Base-rich fens and calcareous spring mires	water
D5	2	Sedge and reedbeds, normally without free-standing water	natgr
D6	2	Inland saline and brackish marshes and reedbeds	water
E	1	Grasslands and lands dominated by forbs, mosses or lichens	natgr
F	1	Heathland, scrub and tundra	natgr
G	1	Woodland, forest and other wooded land	natgr
H	1	Inland unvegetated or sparsely vegetated habitats	natgr
I	1	Regularly or recently cultivated agricultural, horticultural and domestic habitats	agrgr
J1	2	Buildings of cities, towns and villages	hdres
J2	2	Low density buildings	ldres
J3	2	Extractive industrial sites	other
J4	2	Transport networks and other constructed hard-surfaced areas	trans
J4.1	3	Disused road, rail and other constructed hard-surfaced areas	trans
J4.2	3	Road networks	trans
J4.3	3	Rail networks	trans
J4.4	3	Airport runways and aprons	airpt
J4.5	3	Hard-surfaced areas of ports	port
J4.6	3	Pavements and recreation areas	urbgr
J4.7	3	Constructed parts of cemeteries	urbgr
J5	2	Highly artificial man-made waters and associated structures	water
J6	2	Waste deposits	other
X	1	Habitat complexes	natgr

Legend: hdres, high density residential; ldres, low density residential; vldres, very low density residential; indtr, industrial, commercial, public, military and private units; trans, transports; port, port areas; airpt, airport; agrgr, agricultural green; urb, green urban areas, sports and leisure facilities; natgr, natural green.

3.8.8. Walkability

A walkability index for the ATHLETE project will be developed by ISGlobal to quantify how 'walkable' is a buffer of 300 meters around each geocode.

This walkability index is based on the methods of Frank et al[21] and Walk Score[22]. Moreover, it also takes into account the criteria described below:

- Availability of the data
- Objectivity of all input variables
- Resulting index comparable between cohorts

Equation 3 will be used to calculate the walkability index in the HELIX project. It includes the following four components capturing differences in the physical environment. Each index will be converted to deciles before entering to formula to have equal weight:

- Land use Shannon's Evenness Index
- Facility richness
- Population density.
- Connectivity index

Equation 3 Walkability Index (WI)

$$WI = \frac{LUEI + FR + PD + CI}{4}$$

Range: $0 \leq WI \leq 1$

LUEI = Land use Shannon's Evenness Index

FR = Facility richness

PD = Population density

CI = Connectivity index

3.9. Natural spaces including green spaces

Normalized Difference Vegetation Index (NDVI) quantifies vegetation by measuring the difference between near-infrared (which vegetation strongly reflects) and red light (which vegetation absorbs). NDVI values range from +1.0 to -1.0. Areas of barren rock, sand, or snow usually show very low NDVI values (for example, 0.1 or less). Sparse vegetation such as shrubs and grasslands or senescing crops may result in moderate NDVI values (approximately 0.2 to 0.5). High NDVI values (approximately 0.6

[21] Lawrence D. Frank et al., 'Many Pathways from Land Use to Health: Associations between Neighborhood Walkability and Active Transportation, Body Mass Index, and Air Quality', *Journal of the American Planning Association* 72, no. 1 (31 March 2006): 75–87, https://doi.org/10.1080/01944360608976725.
[22] 'Walk Score Terms of Use', accessed 19 December 2016, https://www.walkscore.com/terms-of-use.shtml.

to 0.9) correspond to dense vegetation such as that found in temperate and tropical forests or crops at their peak growth stage. Negative values of NDVI (values approaching -1) correspond to water.

NDVI will be derived from the Landsat 4–5 Thematic Mapper (TM), Landsat 7 Enhanced Thematic Mapper Plus (ETM+), and Landsat 8 Operational Land Imager (OLI)/Thermal Infrared Sensor (TIRS) with 30m x 30m resolution was used to determine the surrounding greenness. The imagery will be selected according to the following criteria: i) cloud cover less than 10 %, ii) Standard Terrain Correction (Level 1T) and iii) greenest period of the year.

Surrounding greenness will be abstracted as the average of NDVI in buffers of 100, 300 and 500 meters[23] around each geocode. Negative values in the images will be reclassified to null values previously.

Furthermore, an indicator for "residential proximity to major green spaces" will be created, as it covers different aspects of green exposure. The EU defined this as living within 300 m of public open area with more than 5000 m^2 (or 15 minute walk)[24]. Also the distance to the nearest green or blue major spaces and the area of this space it will be calculated as other greenness indicators. The Europe-wide "Urban Atlas" (prepared by European Environmental Protection Agency) will be used to extract maps of urban and natural green and blue spaces across HELIX study regions, and if it is not available, local layers will be used instead.

3.10. Traffic

Traffic assessment will be done using local road network with traffic data for all areas (when it is available), except for RHEA. In RHEA data has been collected in a traffic monitoring campaign conducted by ISGlobal as part EXPOsOMICS project to characterize the traffic of the streets of Heraklion will be used.

Traffic variables generated will be as detailed below:

- Trafmajorload: Total traffic load of major roads in a 100m buffer
- Trafload: Total traffic load in a 100m buffer
- Trafnear: Traffic density on nearest road

Another variable to quantify the distance between the geocode and the nearest road will be generated using road network from NAVTEQ:

- Distinvnear: Inverse distance to the nearest road

[23] Payam Dadvand et al., 'Surrounding Greenness and Pregnancy Outcomes in Four Spanish Birth Cohorts', *Environmental Health Perspectives* 120, no. 10 (October 2012): 1481–87, https://doi.org/10.1289/ehp.1205244.
[24] ARI (Ambiente Italia Research Institute), *European Common Indicators Towards a Local Sustainability Profile* (Milan, Italy, 2003), https://www.gdrc.org/uem/footprints/eci_final_report.pdf.

3.11. Social deprivation

Socioeconomic level will be described using country specific deprivation indexes, categorized into tertiles and quintiles, where 1 means less deprived and 3/5 means more deprived.

3.12. Food environment

3.12.1. Unhealthy food environment

Unhealthy food environment variable will be created based on the NAVTEQ database. Among the 100 different subcategories of facilities in the NAVTEQ database we selected the subcategories related to unhealthy food. The unhealthy food environment variable equals the number of unhealthy facilities present divided by the area of the 300 meters buffer (number of facilities / km^2). A higher value indicates a more availability of different unhealthy facilities.

We will compare the mentioned Navteq database with Openstreetmap as well as with commercial and municipality data on food retailers for Sabadell city to assess its completeness, considering healthy and unhealthy food retailers. We will study spatial indicators based on walking time instead of euclidean distance, and others that would allow us to give exposure to unhealthy food environment for routes (such as commuting to school) and areas (such as neighborhoods).

4. Annexes

Annex 1: Standard Operational Procedure for NO2 personal monitoring with palmes passive diffusion tubes

Annex 2: Standard Operational Procedure for GeneActiv

Annex 3: Standard Operational Procedure for personal physical activity monitoring using an Actigraph WGT3X-BT

Annex 4: Standard Operational Procedure for geocoding questionnaire

NO_2 PERSONAL MONITORING WITH PALMES PASSIVE DIFFUSION TUBES

Prepared/revised by: Serena Fossati (prepared) / Gloria Carrasco (revised)

Contact person: Glòria Carrasco

ATHLETE SOP coordinator for personal exposure monitoring: Mark Nieuwenhuijsen (mark.nieuwenhuijsen@isglobal.org)

PURPOSE AND APPLICABILITY

1. PURPOSE AND APPLICABILITY

The purpose of this SOP is to describe the personal monitoring of NO_2 concentration with Palmes passive diffusion tubes for the ATHLETE study.

2. RESPONSIBILITIES AND USERS

1. The ATHLETE SOP coordinator for personal exposure monitoring is responsible for ensuring that new versions of this SOP are available for the relevant members of the project team and its instructions are properly implemented.

2. This SOP will be principally applied by ATHLETE fieldworkers.

3. If the procedures of this SOP are changed, the change has to be documented according to instructions and it has to be communicated to the SOP coordinator.

4. The users of the SOP are obliged to work according to this SOP. All potential deviations in implementing this SOP have to be carefully documented (who changed, when, why, what changes, possible impacts) and reported.

3. DEFINITIONS AND ABBREVIATIONS

FEF: Field Exposure Form for participants to report incidences during monitoring.

SOP: Standard Operating Procedure.

FW: Field Worker

Participant: An adolescent participating in the ATHLETE follow up study.

Participant ID: Each participant is uniquely identified by an ATHLETE identification code.

Diffusion tube: type of passive sampler consisting of a tube, open at one end, with an absorbent at the other (closed) end for absorption of a specific pollutant from the surrounding air.

Diffusion tub ID: Each diffusion tube is uniquely identified by an ATHLETE identification number.

End cap: the plastic cap fixed on the closed end of a diffusion tube, which holds the absorbent-coated grids.

Grid: used here to refer to the small mesh grids used inside the diffusion tube, which are coated with the absorbent TEA.

Membrane: a permeable membrane fixed across the open end of a tube: routinely used in sulphur dioxide tubes to prevent the ingress of particulate sulphate. Has been used experimentally in nitrogen dioxide tubes to reduce interference due to wind effects.

Mesh: used here to indicate a mesh fixed across the open end of a diffusion tube, used experimentally to minimize interference from wind effects (the term "mesh" is used to distinguish this from the "grids" above). This modification is not in routine use at present.

NO_2: Nitrogen dioxide

Passive sampler/ing: methods which absorb the pollutant directly from the ambient air, with no need of power supply.

TEA: Triethanolamine. The reagent used in Palmes-type diffusion tubes as an absorbent for ambient NO_2.

4. EQUIPMENT AND MATERIALS

The nitrogen dioxide (NO_2) passive diffusion tubes will be attached to the study participants backpacks the day of the clinical examination. The tubes will be exposed for 1 week.

4.1. Equipment

NO_2 diffusion tubs (including grids)
Caps
Supports for the tubes
QR codes to identify tubes
Laptop, the same for all monitoring instruments, with an internet access and the clock synchronized to an atomic clock. .

4.2. Materials

Monitoring Sheet for fieldworkers: form to be completed by the FWs when placing the tube and collecting them from the subjects' backpack.
Incidence sheet for the participants: handled to participants to report any incidences during the sampling period.

5. PROCEDURES

5.1. GENERAL OVERVIEW

Palmes diffusion tubes are passive samplers: they consist of small glass tubes containing a chemical reagent to absorb the pollutant to be measured directly from the air. The ATHLETE study will use diffusion tubs distributed by 4Sfera, the Spanish distributor of Gradko's Laboratories. In the case of Gradko's type nitrogen dioxide diffusion tubes, the absorbent used is triethanolamine (TEA). Stainless-steel mesh grids at the closed end of the tube are coated with a water-based or acetone-based solution of this absorbent. They are useful for identifying areas of high NO_2 concentration, particularly when dealing with sources such as traffic emissions, which do not change much from day to day.

5.1.1. Diffusion process in the tubes

Diffusion tubes work by a process called molecular diffusion. During molecular diffusion, compounds will move from an area of high concentration to an area of low concentration. The compounds in the air are at a higher concentration than those in the tube, so the compounds diffuse into the tube and collect on the absorbent at the end of the tube. Because the compounds are absorbed, the low concentration in the tube is maintained, and therefore diffusion continues. The rate that the compounds move into the tube is called the uptake rate. This is a known rate and is used in the calculations during analysis. Many of the tubes are clear as light is required during the absorption process.

5.1.2. Components of the tubes

The following description is only informative, as tubes are prepared in Gradko Lab and sent to ISGlobal, so there is no need to do anything.

5.1.2.1. Tubes

Diffusion tubes should be made of clear or translucent colorless acrylic. Tubes are 7 cm tall and 1.4 cm wide. (figure1)

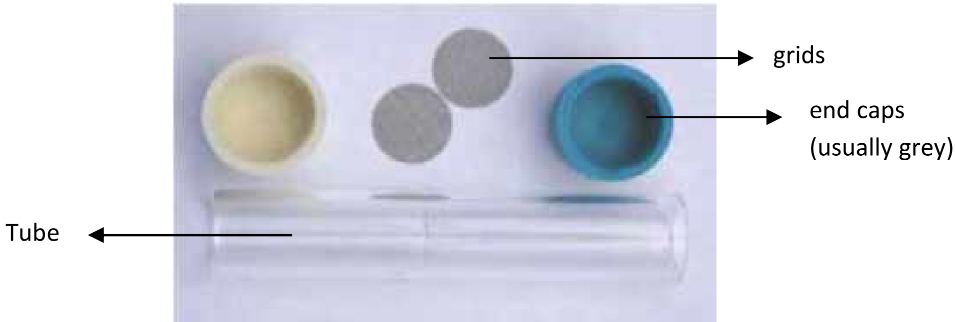


Figure 1. Diffusion Tube Components

5.1.2.2. Grids

Two grids are used per tube, and its material is stainless steel. The mesh size of this grid should be 4x4 per mm^2. The diameter of each circular grid should be slightly larger than the inside diameter of the tube, so that they are fixed firmly in place when the tube is assembled and cannot fall out during exposure.

5.1.2.3. End Caps

The end caps used on the end that holds the grids are opaque flexible plastic of a dark color. Sunlight can degrade the nitrite complex formed when NO_2 combines with the TEA: dark opaque caps minimize this. Colored end caps may be re-used, but must be discarded when the color begins to fade. Any cracked, discolored or split caps must be discarded. As far as possible, use end-caps of one color only in any survey: different colored caps may have different opacity, increasing the uncertainty of the results. Do not, therefore, alternate between different colors in different months. Alternating colored labels should be used instead. If possible, have spare caps in case any cap is missing when collecting the tubes.

Note: Diffusion tubes are ready-made from a supplier, so reject any that arrive with split or damaged end caps.

5.1.2.4. Supports

For ATHLETE, we will have personal clips for the tubes that will be used for personal sampling (figure 2).

Figure 2: NO_2 supports for personal monitoring

5.1.3. General instructions for the tubes

When using NO_2 diffusion tubes, some aspects need to be considered for an optimal usage of the tubes and to ensure good data quality.

5.1.3.1. Shelf life

Tubes have a shelf life of 12 weeks. Tubes must be exposed and returned for analysis within this period so they should be exposed and analyzed within 4 months of preparation. The date of reception and the expiry date (4 months after preparation, 12 weeks of shelf life) should be clearly identified for each tube batch. If preparation/components differ from the standard, the end user should be clearly notified.
Note: in case you need to extend the shelf life, NO_2 tubes in particular allow an extension of its shelf life up to 16 weeks or even a bit more. Please contact the supplier for more info.

5.1.3.2. Tube storage

Tubes should be kept refrigerated before and after exposure and should not be subject to large variations in ambient temperature. Do not exceed the shelf life of 12 weeks if possible. The use of plastic containers and/or sealable clean plastic bags is essential to avoid contamination during transportation. Unexposed tubes should be stored in sealed plastic bags ideally inside a plastic container in a refrigerator.

For the blank tubes, do not remove the tube from the packaging and store them in the same conditions as the sampling tubes. If a refrigerator is not available, they should be stored in a cool dark place without temperature fluctuations.

Tubes and batches of tubes should be labeled appropriately, and enough laboratory blanks should be stored within the laboratory to measure any possible contamination during preparation. It is important that transport blanks (tubes which are not to be exposed and are left capped at all times) are included in any survey. Transport blanks should also be kept in a sealed plastic container as above.

The minimum number of blank tubes per batch: 1 tube (lab blank) each 20 tubes. (If the batch is big (loads of tubes) or there is a lot of budget in the study, then we can consider more than 1. Lab blank is the most important, then the field blank and then the transport blank).

Lab blank – tube that stays in the fridge for the whole time, from the moment that the batch is received until the shipment to the lab. It is important to note the date when you receive the tubes and put them in the fridge and the shipment date when you return the tubes to the lab.

Field blank – tube that is placed with an exposed tube but with the cap on. Before and after being 'exposed', it goes in the fridge like any other participant tubes.

Travel/transport blank - Travel blanks, where applicable, should be identified and their code numbers noted on the exposure details form provided by the laboratory. In case the sampling day is very long, or the tubes are outside the fridge for many hours (for example, all day) and then they come back to the fridge, a transport blank can be done.

5.1.3.3. Labelling the tubes with a QR code provided by the tube suppliers (Note: this is NOT the ATHLETE ID label)

Tubes come with an exposure sheet and a strip of QR codes; these codes are in duplicate: 1 label is for the tube and the other label is to stick it to the *ATHLETE_Exposure_Monitoring_sheet_forFW*.

Figure 4. NO_2 tubes, exposure sheets and QR codes

It is recommended that FWs label the tubes and sheets at the point of placing the tubes; this is a good way of minimizing any possible errors (figure 5). Please make sure the label is securely fixed to the tube. Be aware that these labels are prepared to deal with weather conditions, so they are heavy duty. Do not use any tubes which are cracked, damaged or have uneven ends which may prevent the end caps sealing properly. All tubes should have same dimension in terms of length and internal/external diameter.

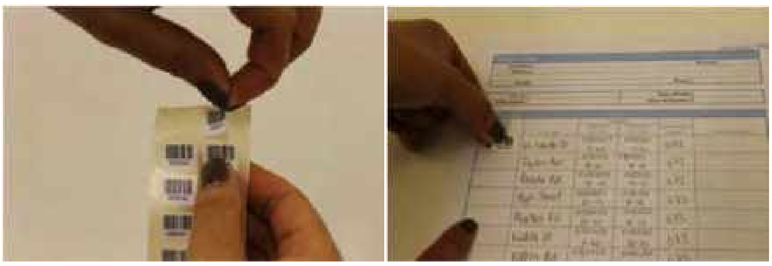


Figure 5. (from top left, clockwise) Take the 1st of the duplicate labels (1) and stick it to the appropriate location on the exposure sheet (2). Then take the 2nd matching label (3) and stick it to the tube exposed at the same location (4).

5.2. MONITORING PROCEDURE

Study subjects will carry a NO_2 tube with them during the study week to measure personal exposure to NO_2. Tubes will be placed on the outside of their backpack.

Participants need to be advised NOT to leave the backpack on the floor whenever possible but leave it on top of an elevated surface (i.e. a table, chair, etc.), ideally at the breathing height, around 1.5m or lower if sitting or sleeping. **Ask participants to avoid placing the backpack on the floor.** It is important that the open end of the tube has free circulation of air, avoiding hair, clothes, etc. blocking the entrance of the air and also not placing the tube (and the rest of the inlets) against a wall (figure 7).

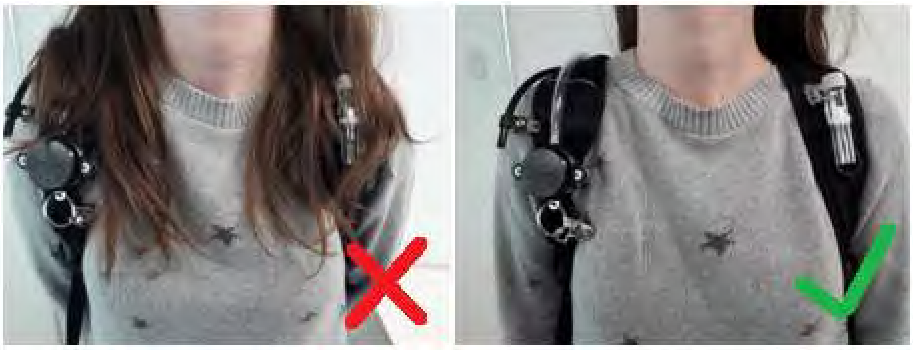


Figure 7. Correct placement of the NO_2 tubes on the backpack.

Study participants will be given an incidence sheet to complete in case they have a problem or an incidence with the NO_2 tubes ("ATHLETE_FieldExposureForm_participants_incidencies" document). An incidence could be i.e. 'tube covered with clothes for 1h' or 'tube moved from shoulder strap to the bottom of the backpack'). They will also be given an information booklet with information of all the devices they will have during the measurement week, so they can check in case they have doubts on how the devices work. They will be also asked to contact FWs in case they need to.

In the case the end of the sampling week does not overlap with the second visit (blood collection), the participant should be asked to leave the tube in place until collection by the fieldworkers.

5.2.1. Exposing the tubes

Remove tubes from the refrigerator on the day that they are to be put out. Take the tubes to the place where the clinical examination is performed in a sealable plastic bag or plastic container. FWs should follow the following procedure:

1. For each participant select one tube and stick the QR code label provided by the tube supplier **(NOTE: this is NOT the ATHLETE ID label)** as you place the tubes.
2. Fill in the *ATHLETE_Exposure_Monitoring_sheet_forFW* clearly with two labesl: 1) the **ATHLETE ID label** (e.g. SAB_14y_C_0001); 2) the **QR code labels provided by the tube supplier**
3. Select the location of the tube in the backpack (the closer to the upper airways the better, ideally at the top of one shoulder strap, see Figure 7) and remove the WHITE cap. Keep the cap in a safe place (put it inside the bag that will be given to the study participants) so it can be used when the sampling week ends. It is advisable to have extra caps in case they get lost.
4. Record the date and time of the start of the exposure period with the time of the laptop (which is synchronized with an atomic clock) on the *ATHLETE_Exposure_Monitoring_sheet_forFW*, and complete the section for NO_2.
5. With the absorbent (colored) end cap uppermost, remove the bottom end cap (usually white or clear in color) and clip the tube into the holder of the clip. Ensure the tube is positioned vertically with its open end downwards during the required sampling period, which will be 1 week for ATHLETE (figure 7).

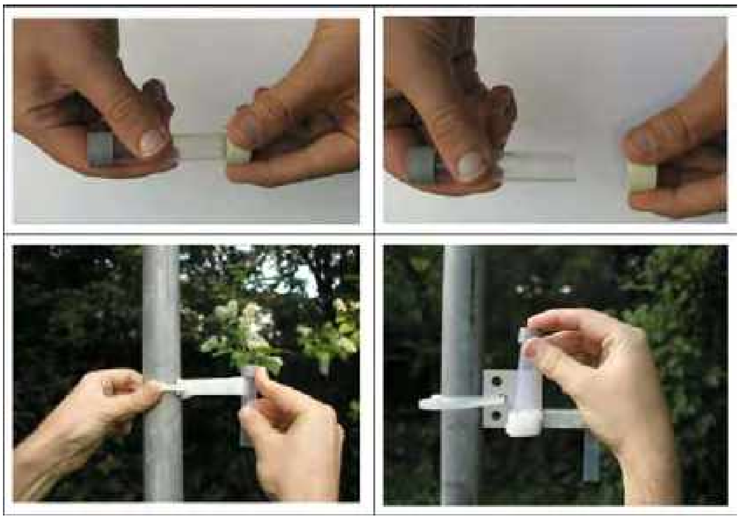


Figure 7. Removing the white cap and placing the diffusion tubes always vertically. This example is for outdoor monitoring, but provides.

5.2.2. Collecting the tubes

After the sampling period, close the tube by putting the WHITE cap back on the tube. Write the date and time down on the *ATHLETE_Exposure_Monitoring_sheet_forFW*. Make a note of any irregularities, anything that might affect, or even invalidate the results such as insects, dirt, or liquid inside the tube. This information will be useful for the laboratory.

5.2.3. Sending the tubes for analysis

Tubes should be returned to the lab for analysis as soon as possible after exposure. However, if you store them in a refrigerator, you can collect tubes for a few weeks and send a big lot to analyze. Send also a paper copy of the *ATHLETE_Exposure_Monitoring_sheet_forFW*, which includes exposure time information. This information will need to be send to 4Sfera, who will send it to the lab via e-mail.

Tubes should be returned in a sealed container, such as the plastic bag that they are received in. They do not need to be sent refrigerated.

Tubes should be sent together with a Lab blank (see the definition above).

Please send the tubes to the following address and let 4Sfera know that you are sending the tubes:

Return address:
Gradko International Ltd,
St Martins House, 77 Wales Street,
Winchester, Hampshire
SO23 0RH
Tel: +44 (0) 1962 860 331
Email: diffusion@gradko.com
enquiries@gradkolab.com

Results are provided within 10 working days or can be fast-tracked by arrangement. The lab determines the concentration of compounds on the tube. This is then used in a calculation with the uptake rate to calculate the average concentration of compounds that were present in the air over the monitoring period. The results are reported in parts per billion (ppb) and micrograms per meter cubed (ugm-3) to allow comparison with health guideline levels. Gradko's reports are e-mailed to ISGlobal within 10 working days of receipt of the samples. This data will be sent out by 4Sfera in a xls and pdf format.

6. QUALITY CONTROL

Data will be checked to make sure the results fall within reasonable values. When tubes experience incidences, results should be carefully interpreted.

Internal quality of the tubes will be also check by having 2 laboratory blanks each time tubes are sent to the Lab in the UK. These tubes will be kept in the fridge properly sealed in plastic bags, along with the non exposed tubes.

7. REFERENCES

Nitrogen dioxide technical data sheet by Gradko.

Diffusion Tubes for Ambient NO_2 Monitoring: Practical Guidance for Laboratories and Users Report to Defra and the Devolved Administrations. ED48673043. Issue 1a. Feb 2008. AEA Energy & Environment.

Long-Term Exposure to Urban Air Pollution and Mortality in a Cohort of More than a Million Adults in Rome. Mapping for change. Air quality mapping Toolkit. NO_2. 2015

Gradko's Technical Data Sheet

Study protocol air pollution exposure assessment for the REGICOR – Air Study population

8. ANNEXES

ATHLETE_FieldExposureForm_participants_incidencies_v1_20200617.docx

ATHLETE_Exposure_Monitoring_sheet_forFW_v1_20200617.docx

ATHLETE Exposure monitoring sheet for FW v1 20200629

Fieldworker:								
SUBJECT ID LABEL				**Visit 1 (clinical examination): __/__/____ Visit 2 (blood collection): __/__/____**				
DEVICES		**SN OR LABEL**	**FW**	**ON**		**OFF**		**COMMENTS**
				DAY	**TIME**	**DAY**	**TIME**	
☐	**Smartphone** e.g. R58K83**W0FQN**		✓ ExpoApp On					
☐	**GeneActive** e.g. Xxx		Wrist: ☐R ☐L					
☐	**Actigraph** e.g. MOS2**A06140080**		Only subsample					

FW QUESTIONS			
DONE?	**YES**	**NO**	**Comments**
Questionnaire	☐	☐	
Geolocation	☐	☐	
Commuting	☐	☐	

NO_2 TUBES						
ATHLETE ID LABEL *e.g. SAB_14y_C_0001s*	**QR CODE LABEL** *NOTE: This is NOT the ATHLETE ID Label*	**QR NUMBER CODE**	**ON**		**OFF**	
			DATE	**TIME**	**DATE**	**TIME**

COMMENTS:

SUBJECT ID LABEL:

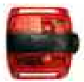
Start date: __/__/_____

PARTICIPANT'S INCIDENCIES

Smartphone

GeneActiv

NO2 tube



Actigraph

	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8	
Date	__/__/__		__/__/__		__/__/__		__/__/__		__/__/__		__/__/__		__/__/__		__/__/__	
Incidence between:	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm
SMARTPHONE																
☐ Switched off																
☐ Not worn																
☐ _____________																
GENEACTIV																
☐ Not worn																
ACTIGRAPH																
☐ Not worn																
NO2 Tube Backpack																
☐ Not worn																
☐ ________________																

SUBJECT ID LABEL:

Start date: __/__/_____

PARTICIPANT'S INCIDENCIES (this second page is only for participants that are collecting data during more than 8 days)


Smartphone


GeneActiv


NO2 tube


Actigraph

	Day 9		Day 10		Day 11		Day 12		Day 13		Day 14	
Date	__/__/__		__/__/__		__/__/__		__/__/__		__/__/__		__/__/__	
Incidence between:	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm
SMARTPHONE												
☐ Switched off												
☐ Not worn												
☐ ____________												
GENEACTIV												
☐ Not worn												
ACTIGRAPH												
☐ Not worn												
NO2 Tube Backpack												
☐ Not worn												
☐ ________________												

SOP GENEActiv

Prepared/revised by: Alba Cabré & Sarah Koch / Maribel Casas

Contact person: Sarah Koch

ATHLETE SOP coordinator for personal exposure monitoring: Mark Nieuwenhuijsen (mark.nieuwenhuijsen@isglobal.org)

1. PURPOSE AND APPLICABILITY

The purpose of this SOP is to describe the personal monitoring of sleeping patterns and physical activity with GENEActiv personal monitors for the ATHLETE study, and also to standardize the operation of GENEActiv.

2. RESPONSIBILITIES AND USERS

1. The ATHLETE SOP coordinator for personal exposure monitoring is responsible for ensuring that new versions of this SOP are available for the relevant members of the project team and its instructions are properly implemented.

2. This SOP will be principally applied by ATHLETE fieldworkers.

3. If the procedures of this SOP are changed, the change has to be documented according to instructions and it has to be communicated to the SOP coordinator.

4. The users of the SOP are obliged to work according to this SOP. All potential deviations in implementing this SOP have to be carefully documented (who changed, when, why, what changes, possible impacts) and reported.

3. DEFINITIONS AND ABBREVIATIONS

MS: Monitoring sheet for fieldworkers to report incidences during field monitoring.

SOP: Standard Operating Procedure.

FW: Field Worker

Participant: An adolescent participating in the ATHLETE follow-up

Subject ID: Each subject is uniquely identified by an ATHELTE identification code.

4. EQUIPMENT AND MATERIALS

The GENEActiv will be worn by study subjects for seven consecutive days (one entire week) during the whole day and night.

4.1. Equipment

The GENEActiv pack includes the device, the charge cradle, and the USB cable to connect the cradle to the computer (Figure 1).

Figure 1. GENEActiv

Each institution is advised to use a laptop, ideally the same laptop for all monitoring instruments, with internet access and laptop time synchronized to an atomic clock to program the GENEActiv device and extract the data after the completion of the data collection period.

4.2. Materials

- USB cables to connect the GENEActiv to the laptop
- MS for FW: form to be completed by the FWs when installing the devices and deploying them from the subjects' home.
- Incidence sheet for the participants: handled to participants to report any incidences during the sampling period.

5. PROCEDURES

One goal of the ATHLETE study is to measure participants' personal sleeping patterns and physical activity levels by using the GENEActiv device (Figure 1). These devices provide objective measurements of human sleeping patterns and physical activity and are used in many research and clinical environments.

5.1. SET UP

1. Install the software on the laptops of the FW.

There are two ways:

- CD provided by the company
- GENEActiv website: https://www.activinsights.com/resources-support/geneactiv/downloads-software/

Remember to also download and install the driver, that you can find on the same homepage. Without the driver, the GeneActiv software will not be able to recognize the cradle with the devices when they are connected to your computer.

2. Before giving the device to the adolescents, the device needs to be set up following these steps:

- Connect the charge cradle to the laptop.
- Open the GENEActiv software in the laptop.

- Plug the device into the charge cradle. Make sure that the device “clicks” into place. The cradle allows plugging and configuring up to 4 devices at the same time and the procedure explained below has to be done for each connected device separately. Sometimes, the charging cradle – device connection can be fairly sensitive. If you do not see the device in the GENEActiv software, remove the device and click it back into the cradle again. Several trials might be necessary.

- Allow GENEActiv devices to charge for 3 hours before using them with the software. A red light on the device will flash to show that it is charging. When it is fully charged, a green light will flash and the device can be removed. Battery status can also be checked in the “Battery Status” box in the right-hand menu. **To ensure that a device records data for the 7 days of measurement, its battery needs to be >80% full**.
- The software displays information about the device and any data previously stored on it will be shown.
- Click “Config. Setup” from the left-hand menu. This page allows you to set recording options and to enter information about the trial and test subject.

- Fill in the following information for each device connected:
  - “Config Operator ID”: introduce the Subject ID.
  - “Measurement Frequency”: the measurements frequency selected will determine the maximum time data can be recorded for, lower frequency = longer time. Select “85.7” (Hz). The “Measurement Period” will be set automatically to 9 days 0 hours.
  - Select “Local PC Time”.
  - In the “Recording Start Mode” box, select when you want to start the recording, selecting “On Button press” and deactivating the option “Allow Stop & Restart”. **This is very important to avoid participants switching off data recording.**
  - Use the “Connected Devices” box to move from the configuration setup window of one device to the other.

  - Go to the “Device” box in the bottom right-handed and click “Select all” and “Erase & Configure”. With this option configuration setup options will be saved for each selected device. **IMPORTANT: this option will delete existing data in the devices. Before configuring devices for new participants, make sure data was saved.**
  - Pop-up windows will advise of any problems (such as mandatory information missing or low battery charge) and warn that configuring will erase any existing data. The configuration will take about 10 seconds and a pop-up will confirm that it has been completed successfully.
  - GENEActiv device/s can now be disconnected and will **start on button press**. Recording will stop after the time selected. **IMPORTANT: Do not forget to press the button on the watch before handing it to the participant, otherwise no data will be recorded.**
  - **IMPORTANT!!** If the device is reconnected to the charge cradle, once it has started recording, it will stop recording and require reconfiguring!!

5.2. PROCEDURE

At the end of the visit 1, place a device to the adolescent's wrist of the non-dominant hand properly configured. Steps to follow:

- Explain to the adolescent that the device is waterproof and that it is not necessary that he takes it our unless he is doing a risk sport that can cause damage to others or himself by wearing it (e.g. karate, etc.)
- Give to the adolescent extra wrist straps in case they need to replace the one they have.
- Give the daily diary to the adolescent (**¡Error! No se encuentra el origen de la referencia.**) and explain how to fill it in. It is important to note in the diary when and why the adolescent stops wearing the device.

After a week, collect the device and the diary at the school. Charge the device until it is fully charged, download the data, save it in the folder of the adolescent, and configure the device for the next adolescent.

5.3. DATA DOWNLOADING

To extract data once recording is complete:

- Open the GENEActiv software and connect the charging cradle to a USB port.
- Insert the device/s into the cradle. The cradle allows plugging and extracting data from up to 4 devices at the same time and the procedure explained below has to be done for each connected device separately.
- Click "Data Extractor" from the left-hand menu. This page previews the first few minutes of recorded data and allows to download data to a chosen file location.

- Chose a file location and extract data with a ".bin" format. Click into "Start Extract". The data can take up to 10 minutes to download and a pop-up will confirm completion.
- Click "Data Converter" from the left-hand menu. This page allows to convert the saved ".bin" file into a ".csv" format file. **But do not forget to also save the .bin file for later data analysis.**

- Select "CSV Converter". Within the "Select input .bin file…", browse and select the previously saved ".bin" file. Then, within the "Select the output .csv file path…", browse the same folder where the ".bin" file was. Click "Start Convert"
- Use the "Connected Devices" box to move from the data extractor window of one device to the other.

- Click "Exit" from the left-hand menu when data extraction is finished. A pop-up message will ask to confirm that we want to exit de software. If we reply YES, the software will close.

5.4. DATA STORAGE

Data will be always stored under the ID number of the participant. FWs will store the data first on their laptop, then copy it to an external hard drive and finally uploaded to a server.

6. QUALITY CONTROL

6.1. Physical activity validation

Physical activity data will be checked to make sure the device is reading properly, so the energy expenditure in METs will be checked to find any inconsistencies. Light intensity activities are those < 3 MET, moderate intensity activities 3-6 MET, and vigorous intensity activities > 6 MET.

6.2. Wearing time validation

Wearing time should preferably be around 16 hours per day for the whole week of measurements; however, a minimum of 10 hours is needed to have a valid day. ATHLETE will not ask participants to re-wear the devices in case this criterion is not achieved.

Data and wearing time will be checked a posteriori by the ATHLETE data manager using the statistical computing program R.

7. REFERENCES

GENEActiv website: https://www.activinsights.com/resources-support/geneactiv/downloads-software

8. ANNEXES

ATHLETE_FieldExposureForm_participants_incidencies.docx
ATHLETE_Exposure_Monitoring_sheet_forFW_version.docx

PERSONAL PHYSICAL ACTIVITY MONITORING USING AN ACTIGRAPH wGT3X-BT

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ATHLETE SOP coordinator for personal exposure monitoring: Mark Nieuwenhuijsen (mark.nieuwenhuijsen@isglobal.org)

1. PURPOSE AND APPLICABILITY

The purpose of this SOP is to describe the personal monitoring of physical activity with ActiGraph personal monitors for the Athlete study, and also to standardize the operation of ActiGraph GT3X-BT.

2. RESPONSIBILITIES AND USERS

1. The ATHLETE SOP coordinator for personal exposure monitoring is responsible for ensuring that new versions of this SOP are available for the relevant members of the project team and its instructions are properly implemented.

2. This SOP will be principally applied by ATHLETE fieldworkers.

3. If the procedures of this SOP are changed, the change has to be documented according to instructions and it has to be communicated to the SOP coordinator.

4. The users of the SOP are obliged to work according to this SOP. All potential deviations in implementing this SOP have to be carefully documented (who changed, when, why, what changes, possible impacts) and reported.

3. DEFINITIONS AND ABBREVIATIONS

FEF: Field Exposure Form for participants to report incidences during monitoring.

MS: Monitoring sheet for fieldworkers to report incidences during field monitoring.

SOP: Standard Operating Procedure.

FW: Field Worker

MET: 1 MET (Metabolic Equivalent of Task) is defined as the amount of oxygen consumed while sitting at rest and is equal to 3.5 ml O_2 per kg body weight x min. The MET concept represents a simple, practical, and easily understood procedure for expressing the energy cost of physical activities as a multiple of the resting metabolic rate.

Participant: An adolescent participating in the ATHLETE follow-up

Subject ID: Each subject is uniquely identified by an ATHELTE identification code.

4. EQUIPMENT AND MATERIALS

The ActiGraph will be worn by study subjects for seven consecutive days (one entire week) during waking hours.

4.1. Equipment

ActiGraph wGT3X-BT model
ActiLife software: https://www.actigraphcorp.com/support/software/.
Laptop, the same for all monitoring instruments, with internet access and laptop time synchronized to an atomic clock.

4.2. Materials

- Spibelt to attach the ActiGraph (device must be on the right-hand side of the belt)
- USB cables to connect the ActiGraph to the laptop
- Monitoring sheet for fieldworkers: form to be completed by the FWs when installing the devices and deploying them from the subjects' home.
- Incidence sheet for the participants: handled to participants to report any incidences during the sampling period.

5. PROCEDURES

5.1. GENERAL OVERVIEW

One goal of the ATHLETE study is to measure participants' personal physical activity levels by using the wGT3X-BT (Figure 1). These devices provide objective measurements of human physical activity and are used in many research and clinical environments.

5.1.1. Physical activity

The ActiGraph wGT3X-BT are the activity monitors used in the ATHLETE study to capture and record continuous, high resolution physical activity. Monitors contain a 3-axis micro-electro-mechanical system (MEMS) accelerometer with a dynamic range of +/- 8 G. The acceleration data is sampled by a 12 bit analog to digital converter at rates ranging from 30 Hz to 100 Hz (user selectable) and stored in a raw, non-filtered/accumulated format in the units of gravity (G's). This data is stored directly into non-volatile flash memory.

The wGT3X-BT device can be worn at the waist or on the non-dominant wrist using adjustable belts or wrist straps. The appropriate wear location is dependent on specific research objectives of each study. For ATHLETE, ActiGraph will be worn on the waist, sitting on top of the hipbone using a SPIbelt (figure 2).

Figure 1. ActiGraph wGT3X-BT

Figure 2. SPIbelt

5.1.2. Device waterproofness

The wGT3X-BT is water resistant on immersion in one meter of water for up to 30 minutes if the USB port is properly closed, otherwise, water can get into the device and damage the electronics. Since this study deploys the devices to many different participants, we will treat the devices as **non-waterproof** to avoid any possible damage. Participants should be advised that the devices need to be taken off and removed when showering, bathing, or swimming. Immediately after taking the device off (due to being in contact with water, for example, for showering), the devices should be put back on and worn again so data is collected.

5.1.3. Battery life and LED decoding

ActiGraph battery can last up to 25 days when wireless is disabled and with a 30Hz sampling rate. At a higher sampling rates, battery life is 19 days with a data storage capacity of 16 days of data recording. However, this depends on the previous usage for each device; therefore, it is worth testing each single device before starting the measurements. The minimal requirements for the ATHELTE study is to allow for data collection for 7 full days at a sampling frequency of 30 Hz.

The ActiGraph contains a rechargeable lithium-ion battery that should be fully charged before initialization and deployment to subjects. The ActiGraph software, ActiLife, will not initialize a device if the battery has dropped below 3.1 volts while in use as the device will not have sufficient power to collect data and will warn the user through a series of coded flashes (Table 1 and Table 2). The battery level, reported in volts, can be viewed at any time by starting the ActiLife software and plugging the device in.

The ActiGraph's battery has a maximum voltage of approximately 4.20 volts. At 3.1 volts the devices enter a *Low Voltage Mode* state (called HALT mode); the battery discharges beyond a point of being able to power the device. In this mode, all important variables and data are stored in flash memory to secure the device download. Because the device's internal clock stops in HALT mode, the device cannot be recharged and redeployed; the device must first be downloaded and reinitialized to continue use. Please note that ActiGraph will not allow initialization if the voltage is below 3.85 volts.

Neither a PC nor any software are required to charge the device. Charging the device is automatic and is accomplished by connecting the device to a standard USB port. It takes no more than 3 hours to charge a fully depleted battery.

<u>Charging instructions:</u>

1. Unscrew the USB port cover by turning it counterclockwise with the triangle tool (Figure 3).
2. Connect the ActiGraph to a laptop/PC using a USB cable.
3. While charging, the ActiGraph will display a flashing green LED.
4. The device is fully charged once the green LED stays on steady, and 100% battery will be displayed on the ActiLife Software. Select 'Refresh' to update the voltage level during charging.
5. Screw the USB port properly so it is protected from water and dust.

Figure 3. Actigraph USB port to charge and download data

5.1.4. Battery Conditioning and Storage

While Lithium Ion batteries provide the highest energy density on the market, their shelf life can be negatively impacted if not properly stored during periods of no use. To slow the aging of the Lithium Ion battery, it is recommended that devices be stored in a partially charged state (40 – 60% battery capacity is ideal) in low ambient temperatures. It is important then to charge the devices even when they are not being used.

Note: If a computer is not available or if multiple devices need to be recharged, a self-powered USB hub can be used. **IMPORTANT:** Remember units must be charged fully before their use.

Table 1. Flashing codes when the device **IS** connected to a PC

RED LED (Fault Indicator)

2 Flashes	Li-Ion Battery is Faulty
3 Flashes	A hardware failure occurred while recording data. Contact customer support

GREEN LED

1 Flash	Battery Charging
Multiple Flashes	Communicating with PC via USB
Steady On	Battery Fully Charged

Table 2. Flashing code when the device is **NOT** connected to a PC

RED LED (Fault Indicator)

No Flashing (LED Off)	Normal operating condition or battery dead
2 Flashes	Low Battery (use ActiLife software to check for remaining battery life). The unit needs to be recharged.
3 Flashes	Unexpected Battery Failure (Temporary battery power loss) - or - - Battery Level has fallen below 3.1V and the unit has entered Halt Mode

GREEN LED

No Flashing (LED Off)	Actively collecting data (“Flash Mode” disabled) or battery dead
1 Flash	- Delay before start mode (the LED always flashes prior to starting data collection) - Actively taking data ("Flash Mode" enabled – not recommended)
2 Flashes	N/A
3 Flashes	- End of memory reached (Device no longer collecting data) - Battery died while unit was in delay before start mode (no data collected on device)

Note: The Red LED will ALWAYS flash to indicate LOW BATTERY regardless of whether "Flash Mode" is enabled or disabled. If a “stop time” (optional) has been reached, the Green LED will stop flashing all together regardless of its previous state.

5.1.5. Installing ActiLife software

You must be running ActiLife version 6.13.3 or higher to operate the wGT3X-BT device.

1. Go to: http://www.actigraphcorp.com/actilife
2. Click the 'Download' button. Follow the instructions to install the ActiLife software on your PC. When prompted, enter the ActiLife license key that was provided at the time of purchase to complete the installation. Ask the coordinator in case you need more information.

Note: The ActiLife FULL version and ActiLife LITE can both be used to initialize and download data from the wGT3X-BT. However, the ActiLife FULL version is required to view and/or process the collected data. FWs will have a LITE version, and the Coordinator will keep the FULL version.

5.2. MONITORING PROCEDURE

This section describes the procedure to properly configure and hand out the device to the participants before the monitoring week. Configuration of the device will be performed with a laptop before handing the ActiGraph to the participant.

The ActiGraph wGT3X+ is a triaxial accelerometer which can store raw acceleration data for long periods of time. The data reflect acceleration vectors with gravity as a reference point (vertical axis, -1G in Axis1). In three perpendicular axis vectors are collected and the vector sum is calculated. The latter is done on a minute-by-minute basis.

For the ATHLETE project, devices are worn on the waist, sitting just above the participant’s right hipbone. Data is collected at a frequency of 30Hz.

5.2.1. Setting up the ActiGraph and starting data collection

1. Open the ActiLife software.

2. Connect the ActiGraph to the PC/laptop using the USB cable. The monitor will appear in the grid under the 'Devices' tab (Figure 4). Please check the information on the battery status. The information shown is the information recorded for the previous participant (which you will have already downloaded).

Figure 4. Overview of the ActiLife software with one ActiGraph wGT3X-BT device connected.

3. Select '**Initialize**.' A submenu will open to display several initialization options. Select '**Regular Initialization'** from the submenu. A dialog box will open to display the initialization parameters listed below (Table 3, Figure 5). The most commonly used initialization parameters are pre-selected as system defaults. However, now it's time to initialize the parameters if you choose a different option than the default.

Table 3. Parameters when configuring the device.

Parametre	Setting
Use Stop Time?	Unticked
Sample Rate	30Hz
Delay Mode LED	Unticked
Data collection LED	Unticked
Enable wireless	Unticked
Idle Sleep Mode	Disabled

For "**Select start time**", select an approximate time when the device will be fitted to the participant. "**Use stop time**" should not be selected, and the device should record until the battery is depleted, the memory capacity is full, or until the participant returns the device and data is downloaded and the device reinitialized. Check that the device time is displaying the "**Use local computer time**", which will be synchronized with an atomic clock. The laptop time needs to get an internet connection at least once a day to get updated the atomic time.

Select the device "**Sampling Rate"** at 30Hz. The sampling rate is the number of times per second that the activity monitor will record data. Note that higher sampling rates will result in higher data fidelity but will reduce the device's storage capacity and battery life. Then click on "**Enter Subject Info**".

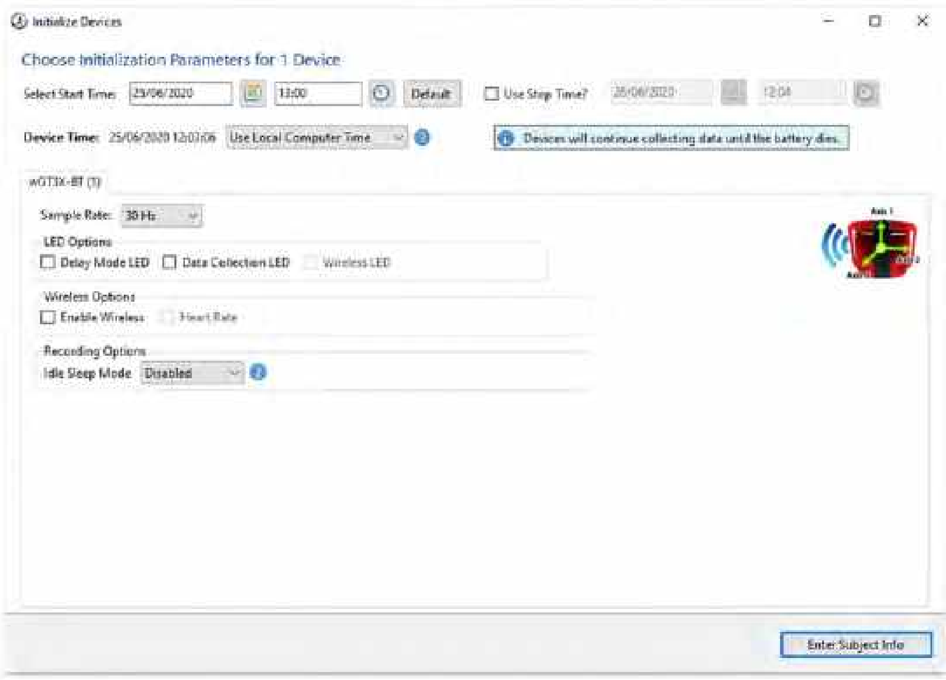


Figure 5. Initialization of the ActiGraph.

A screen with some other recoding options is shown (Figure 6). Add the ATHLETE participant ID in the "**Subject info**" box, and "**Limb**" must be on the waist. If preferred, you can enter some biometric information and wear details when setting, when downloading or at data analysis. However, for ATHELTE we will not introduce any other subject information. Then select "**Initialize 1 Device**".

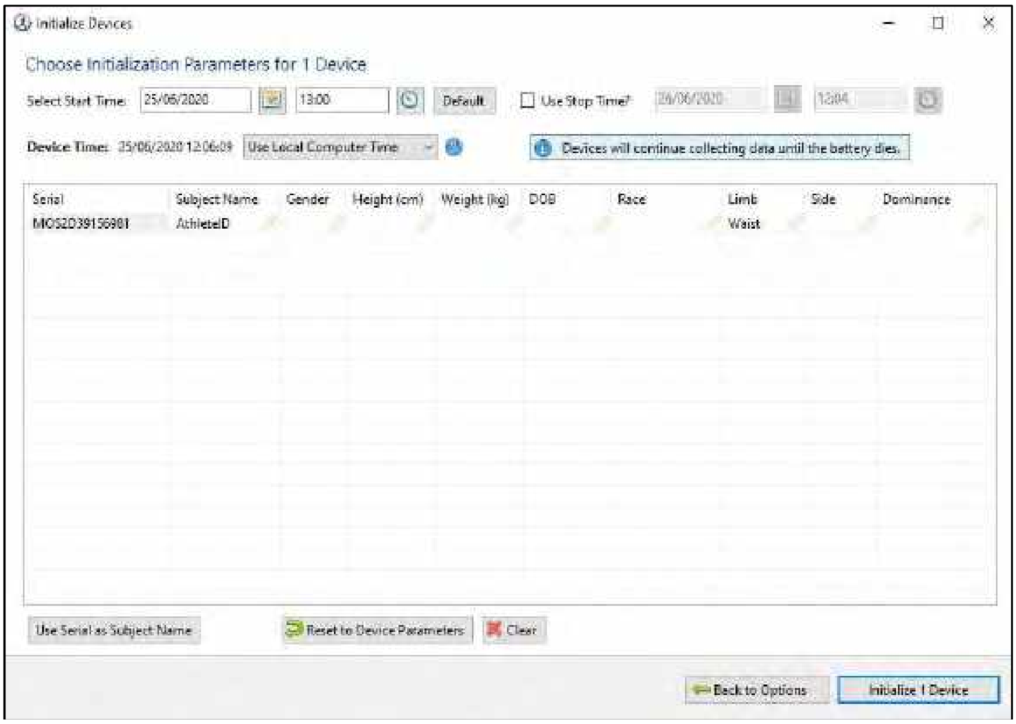


Figure 6. Recording options and subject information

After selecting “Initialize 1 Device”, a progress bar in the devices grid will indicate when the initialization process is completed. Please check the battery level again in case it needs further charging.

After the initialization is complete, unplug the ActiGraph and close the USB cap by turning it clockwise with a clip tool. Be careful not to overtighten it. The device will begin collecting data when the selected start time elapses and will continue to collect data until the device is downloaded and reinitialized.

Note: Multiple devices can be initialized simultaneously using one or more ActiGraph approved charging hubs. In this case, all devices will be programmed with the same initialization parameters and the Subject Info grid will display serial numbers of all connected devices for assignment.

5.2.2. Wearing the Device

Subjects should be instructed to wear the device strapped securely on the belt, on top of their right hipbone. The ActiGraph is waterproof ONLY when the cap is properly locked, so we will ask participants NOT TO WEAR the device while they are in contact with water, so they should remove it before showering/bathing/swimming.

Attach the SPIBelt waist belt to the participant and adjust the straps until the belt fits snugly around the waist. Position the GT3X-BT on the SPIbelt so it is facing upwards (Figure 7). The USB port cover **must** be positioned upwards/towards the participant’s head. The ActiGraph wGT3X-BT must be sitting just above the participant’s **RIGHT hipbone** (Figure 8). Double check that the USB port cover is facing upwards.

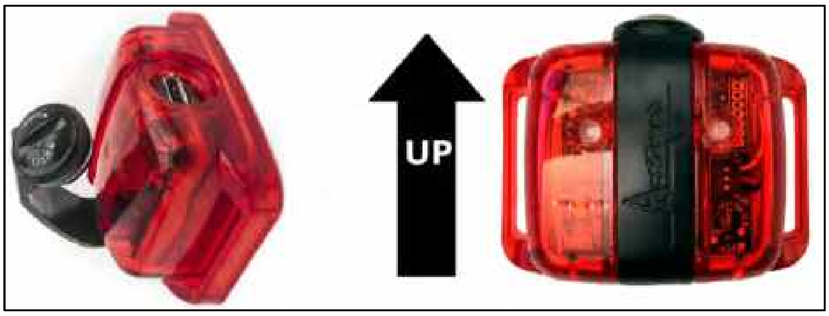


Figure 7. ActiGraph must be facing upwards.

The device should be worn during the day (**<u>all waking hours</u>**) and the belt removed each night before bed and reattached each morning just after getting out of bed or after showering/bathing. The participant should be instructed to fasten the belt snugly around the waist and position the wGT3X-BT USB port cover **facing up** on the right hipbone.

Figure 8. Location of the ActiGraph on the right hipbone on a SPIbelt.

Study participants will be given an incidence sheet to complete in case they have a problem or an incidence with the ActiGraph ("ATHLETE_FieldExposureForm_participants_incidencies" document) or any other study devices. An incidence could be *i.e.* 'swimming in the pool/sea'; taking the ActiGraph off to shower does not need to be noted on the sheet, only activities that take longer than 15min.

They will also be given a copy of any study specific instructions for wearable devices to take home (including a study specific contact phone number) with information of all the devices they will have during the measurement week, so they can check in case they have doubts on how the devices work. They will be also asked to contact FWs in case they need to.

The ActiGraphs should be cleaned after each deployment using an alcohol-based solution or wipe. SPIbelts should be handwashed.

5.3. DATA DOWNLOADING

Data will be downloaded at the end of the monitoring week, right after collecting the devices from the participant.

1. Open the ActiLife Software.
2. Connect the ActiGraph to the PC/laptop using the USB cable. The monitor will appear in the grid under the 'Devices' tab (figure 9).
3. Verify that the box of the device is checked and select **'Download'** from the taskbar menu (Figure 9).
4. A dialog box will open to display the download options listed below (Figure 10). The most commonly used download parameters are pre-selected as defaults. For ATHLETE, use the options shown in Table 4. Epoch will be set at 10 seconds.

Figure 9. Once the device is connected, the software will display it and now it is ready for download.

Table 4. Downloading data parameters

Parametre	Setting
Download name convention	subject name, start date
Create Clinical Report on Download for ActiSleep Monitor(s)	Unticked
Create AGD File	Ticked
Epoch	10 seconds
# of Axis	3
Steps	Ticked
Lux	Unticked
Inclinometre	Ticked
Low Frequency Exptension	Ticked
Add Biometric and user information	

Select where you want to download the files by changing the path in “Change Location”. **“Download Naming Convention”** provides a list of file name formats; choose “Subject Name, Start Date” as the subject name (the participant ID) was previously introduced. In **“Download Options”** choose “Create AGD File”. Then an AGD file, required for data scoring, will be automatically created when download.

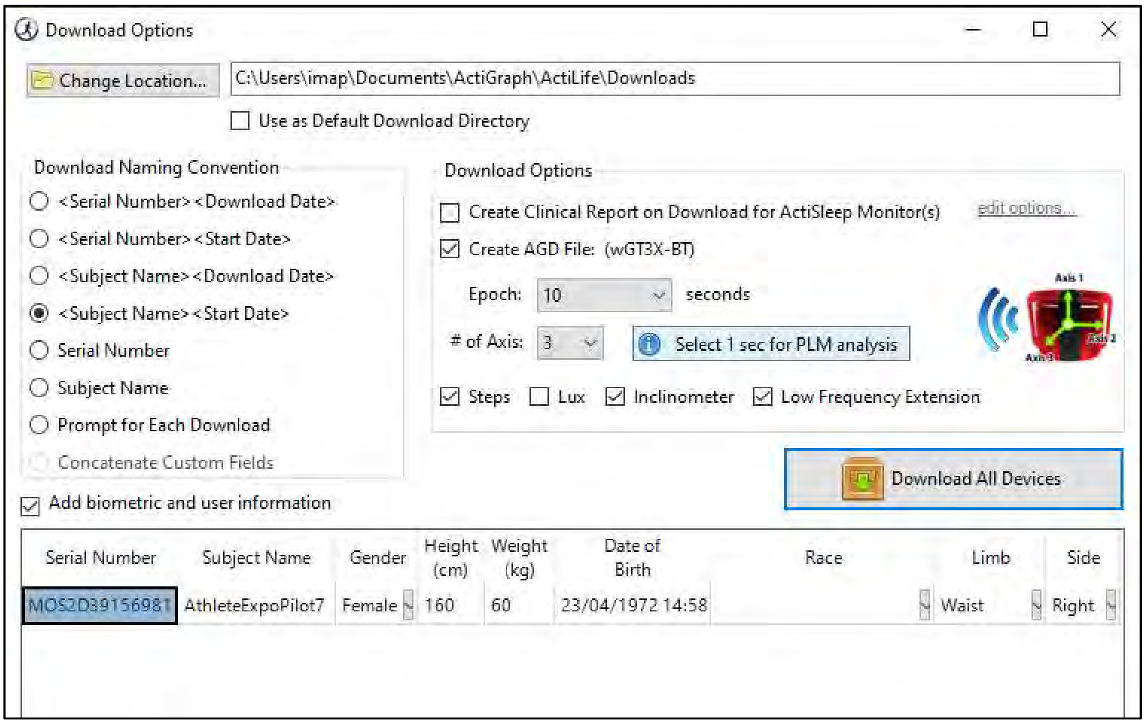


Figure 10. Downloading the data using ActiLife Software.

Select the desired epoch length for the AGD file. The epoch length represents the amount of time the raw acceleration data is summed after the filter is applied. It is typically 10sec. Select which axes of data should be included in AGD file (*1 Axis=Y; 2 Axis=X,Y; 3 Axis=X,Y,Z). **Select 3 axes.*** Select “Steps” in order to include step count data in AGD file. Select ”Inclinometer” in order to include positional data (standing, sitting, or lying down and when the device has been removed) based on device orientation in the AGD file. Select “Low Frequency Extension” to apply a low frequency filter extension to AGD file. Click on “**Download all devices**”.

Note: The Low Frequency Extension option should only be used in very specific cases where physical activity is at such a low level that it might otherwise be eliminated with our normal filter. An example would be very slow shuffling movements, common in elderly populations.

A customizable PDF report containing summary data can be created with the FULL license. Subject measures and scoring algorithms can be selected by clicking 'edit options.'

Data has now successfully been downloaded from the ActiGraph and can be cleaned and scored using the analysis tools in ActiLife. The two raw data files created are **1) ID.gt3x and 2) ID10sec.agd files:**

1. ActiLife GT3X File (RAW Device Data) (.gt3x)
2. ActiLife AGD File (Accumulated Device Data every 10 seconds) (.agd)

When using the FULL license, and the download is complete, a 'finished downloading' link will appear (figure 11). Click this link to reveal options to view data, export the raw data file, and navigate to the download folder. Ensure the export settings are as show in Figure 12 then click ‘*Export RAW Files*’ to complete the export.

LITE license does not allow doing that, so you can convert the data once data collection of the study is ended (ask your coordinator for a FULL license). You can upload files and then .agd files can be exported to .csv by going to File -> import/export -> AGD -> Data Table (.CSV) (Figure 13). Save the data with the ID of the participant.

The collected data will remain on the ActiGraph device until it is reinitialized. For more information on data scoring and analysis using the ActiLife software, see the ActiLife User's Manual.

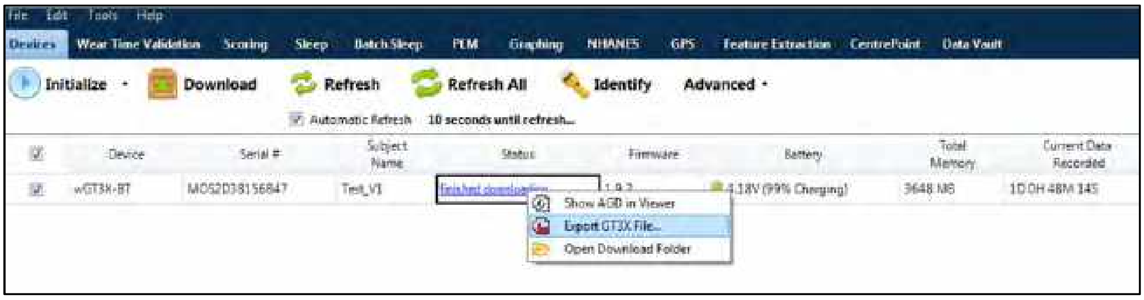


Figure 11. Exporting data with the FULL license.

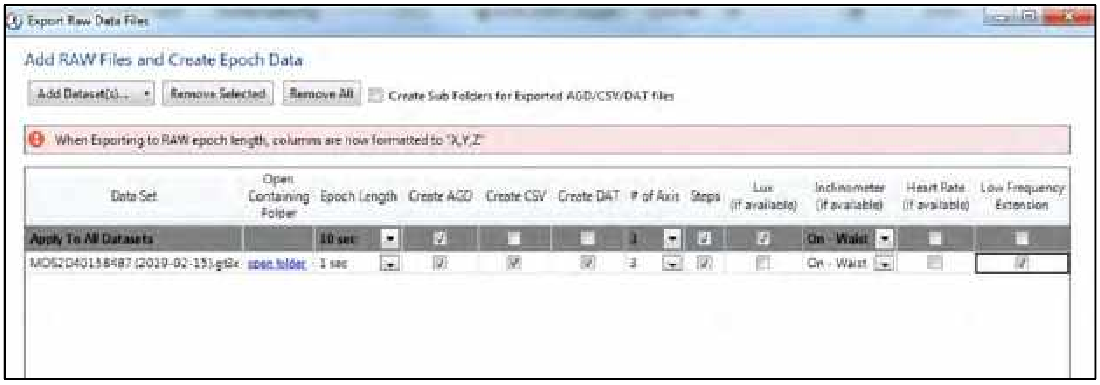


Figure 12. Creating epoch data from raw files.

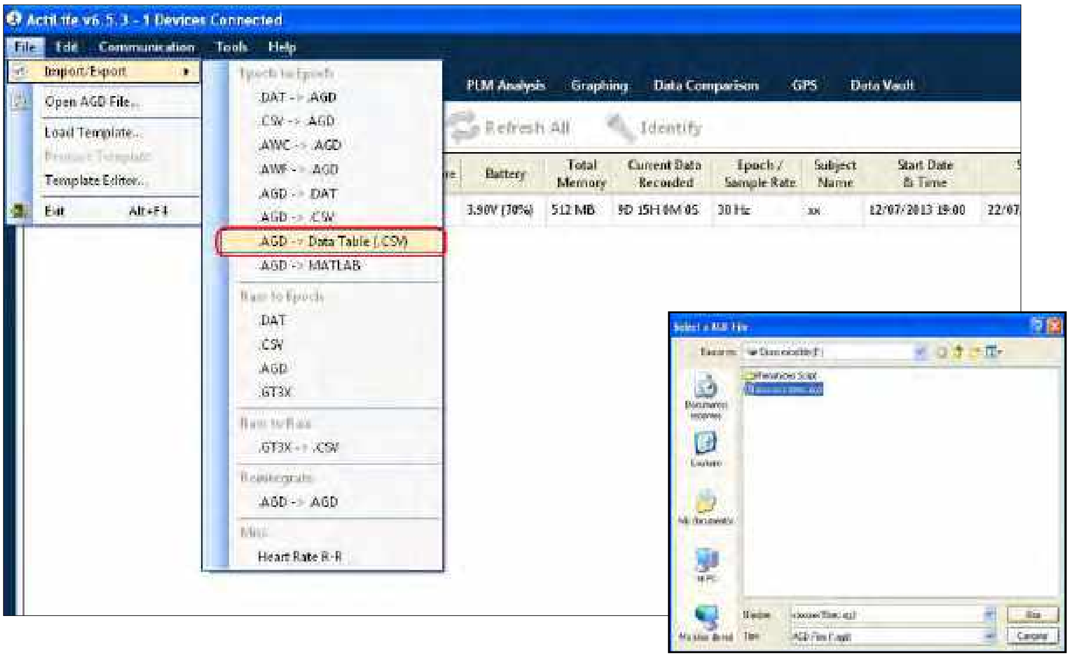


Figure 13. Exporting the .agd file to a .csv file

Navigate to the participant folder, and double check the GT3X, AGD, CSV and DAT files have all been saved (this is once you have converted the files using the FULL license). The GT3X file (ActiLife GT3X File (RAW Device Data, .gt3x)) is the raw data and **MUST BE DOWNLOADED** and saved correctly to extract and analyse the data.

5.4. DATA STORAGE

Data will be always stored under the ID number of the participant. FWs will store the data first on their laptop, then copy it to an external hard drive and finally uploaded to a server.

6. QUALITY CONTROL

6.1. Physical activity validation

Physical activity data will be checked to make sure the device is reading properly, so the energy expenditure in METs will be checked to find any inconsistencies. Light intensity activities are those < 3 MET, moderate intensity activities 3-6 MET, and vigorous intensity activities > 6 MET.

6.2. Wearing time validation

Wearing time should preferably be around 16 hours per day for the whole week of measurements; however, a minimum of 10 hours is needed to have a valid day. ATHLETE will not ask participants to re-wear the devices in case this criterion is not achieved.

Data and wearing time will be checked a posteriori by the ATHLETE data manager using the statistical computing program R.

7. REFERENCES

http://s3.amazonaws.com/actigraphcorp.com/wp-content/uploads/2018/02/22094126/GT3X-wGT3X-Device-Manual-110315.pdf

https://www.actigraphcorp.com/actigraph-wgt3x-bt/

ActiLife Manual: https://s3.amazonaws.com/actigraphcorp.com/wp-content/uploads/2018/02/22094137/SFT12DOC13-ActiLife-6-Users-Manual-Rev-A-110315.pdf

iMAP project ActiGraph Protocol: SOP003_ActiGraph GT3X-BT_v3_20191204

8. ANNEXES

ATHLETE_FieldExposureForm_participants_incidencies.docx
ATHLETE_Exposure_Monitoring_sheet_forFW_version.docx

ATHLETE Exposure monitoring sheet for FW v1 20200629

Fieldworker:

SUBJECT ID LABEL	Visit 1 (clinical examination): __/__/____ Visit 2 (blood collection): __/__/____

DEVICES		SN OR LABEL	FW	ON		OFF		COMMENTS
				DAY	TIME	DAY	TIME	
☐	**Smartphone** e.g. R58K83W0FQN		✓ ExpoApp On					
☐	**GeneActive** e.g. Xxx		Wrist: ☐R ☐L					
☐	**Actigraph** e.g. MOS2A06140080		Only subsample					

FW QUESTIONS			
DONE?	YES	NO	Comments
Questionnaire	☐	☐	
Geolocation	☐	☐	
Commuting	☐	☐	

NO_2 TUBES						
ATHLETE ID LABEL *e.g. SAB_14y_C_0001s*	QR CODE LABEL *NOTE: This is NOT the ATHLETE ID Label*	QR NUMBER CODE	ON		OFF	
			DATE	TIME	DATE	TIME

COMMENTS:

SUBJECT ID LABEL:

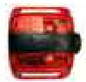
Start date: __/__/_____

PARTICIPANT'S INCIDENCIES

Smartphone

GeneActiv

NO2 tube



Actigraph

	Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7		Day 8	
Date	__/__/__		__/__/__		__/__/__		__/__/__		__/__/__		__/__/__		__/__/__		__/__/__	
Incidence between:	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm
SMARTPHONE																
□ Switched off																
□ Not worn																
□ ____________																
GENEACTIV																
□ Not worn																
ACTIGRAPH																
□ Not worn																
NO2 Tube Backpack																
□ Not worn																
□ ________________																

ATHLETE
The Exposome from Evidence to Translation

SUBJECT ID LABEL: ____________ **Start date:** __/__/_____

PARTICIPANT'S INCIDENCIES (this second page is only for participants that are collecting data during more than 8 days)


Smartphone


GeneActiv


NO2 tube


Actigraph

	Day 9		Day 10		Day 11		Day 12		Day 13		Day 14	
Date	__/__/__		__/__/__		__/__/__		__/__/__		__/__/__		__/__/__	
Incidence between:	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm	From hh:mm	To hh:mm
SMARTPHONE												
☐ Switched off												
☐ Not worn												
☐ ____________												
GENEACTIV												
☐ Not worn												
ACTIGRAPH												
☐ Not worn												
NO2 Tube Backpack												
☐ Not worn												
☐ ________________												

GEOCODING QUESTIONNAIRE

Prepared/revised by: Montserrat de Castro, Júlia Sangüesa, Maribel Casas
Contact person: Montserrat de Castro
ATHLETE SOP coordinator: Maribel Casas (maribel.casas@isglobal.org)

1. PURPOSE AND APPLICABILITY

The purpose of this SOP is to describe a detailed procedure for geocoding home addresses, school addresses and the usual commuting routes from home to school for all the subcohort participants.

2. RESPONSIBILITIES AND USERS

1. The ATHLETE SOP coordinator is responsible for ensuring that new versions of this SOP are available for the relevant members of the project team and its instructions are properly implemented.
2. This SOP will be principally applied by ATHLETE fieldworkers.
3. If the procedures of this SOP are changed, the change has to be documented according to instructions and it has to be communicated to the SOP coordinator.
4. The users of the SOP are obliged to work according to this SOP. All potential deviations in implementing this SOP have to be carefully documented (who changed, when, why, what changes, possible impacts) and reported.

3. DEFINITIONS AND ABBREVIATIONS

SOP:	Standard Operating Procedure
Participant:	An adolescent participating in the Athlete follow-up

4. EQUIPMENT AND MATERIALS

4.1. Equipment

It will be needed a computer or laptop with internet connection. The operational system could be Windows, macOS or Linux.

4.2. Materials

The software used in the present procedure is QGIS. QGIS is a free and open source Geographic Information System (GIS) that is easily downloadable and user friendly. QGIS version 3.12.3 'București' will be used (more information here: https://www.qgis.org/en/site/index.html).

It is important that you get familiar with the program before interviewing participants in order to save time and to reduce errors.

A folder named "GEOCODING_QUESTIONNAIRE" will be provided which contains all data you need to install QGIS software and fill Geocoding Questionnaire for each participant. Into this folder you will find 2 folders:

- PROJECT_0

- SOFTWARE

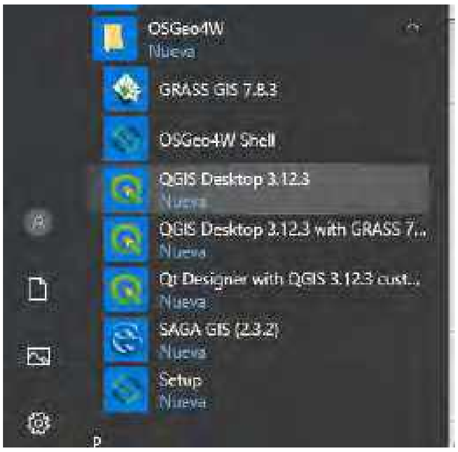
5. PROCEDURES

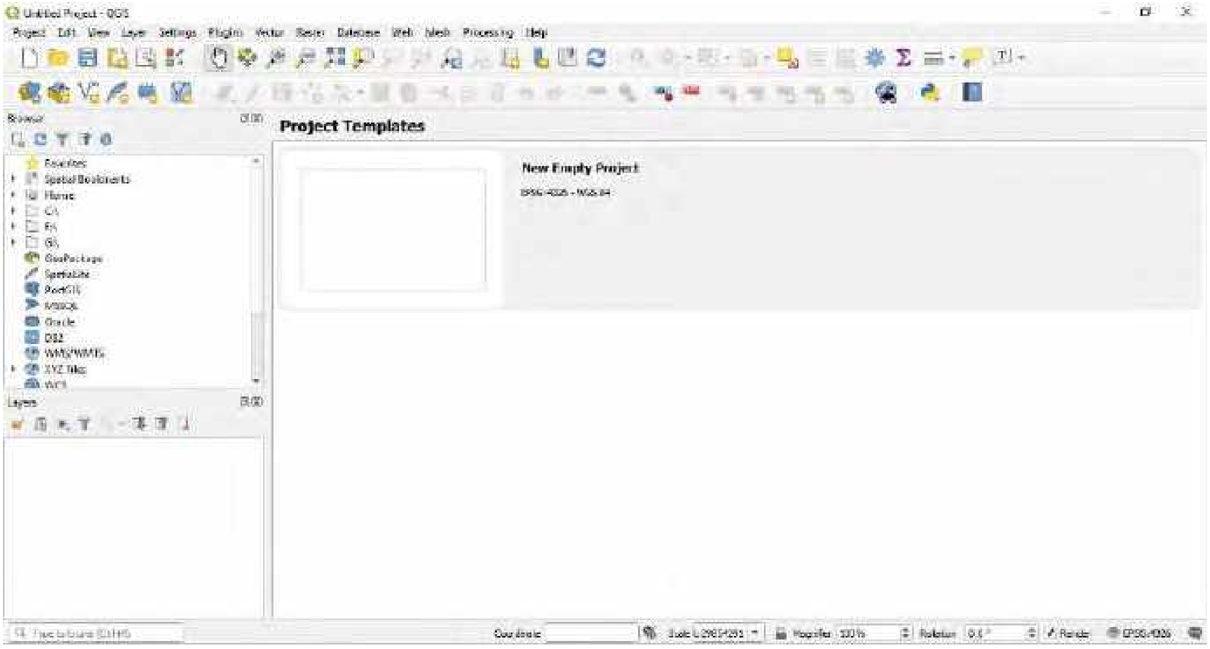
5.1. Prepare software

5.1.1. Install software

1. First of all, copy the "GEOCODING_QUESTIONNAIRE" folder provided by ISGLOBAL into your computer.
2. To install QGIS: double click on QGIS executable file you will find in GEOCODING_QUESTIONNAIRE\SOFTWARE folder. There are two executable files: 32 and 64 bit. You need to choose the file depending on your computer characteristics:
    a. osgeo4w-setup-x86.exe → 32 bit
    b. osgeo4w-setup-x86_64.exe → 64 bit

3. Open QGIS Desktop 3.12.3 and be sure it works.

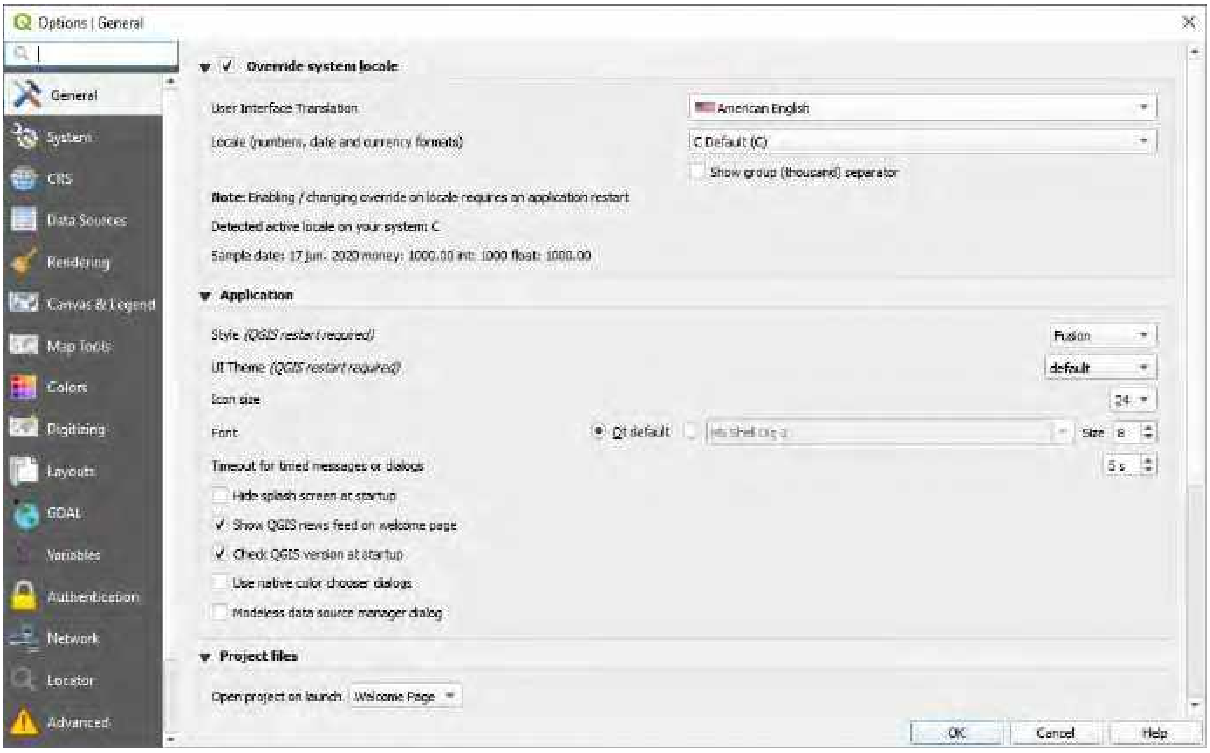




4. Now, you can remove GEOCODING_QUESTIONNAIRE\SOFTWARE folder if you want (you won't need those files anymore).

5.1.2. Change language (optional)

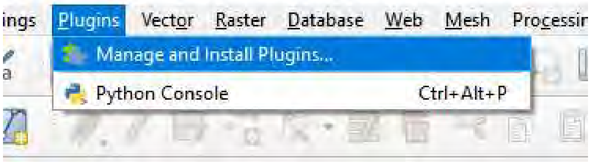
1. Click on the menu bar Settings ▸ Options.
2. Check "Override system locale" and set your language in there.



3. Restart QGIS to reload it.

5.1.3. Plugin installation

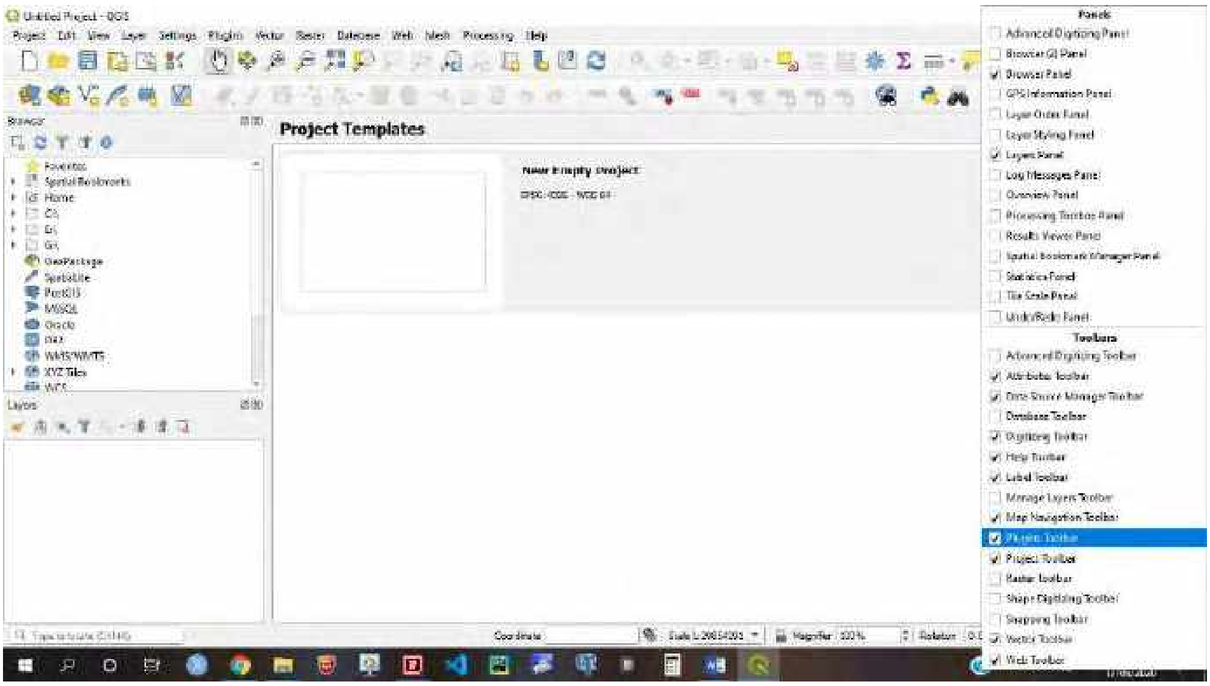
1. To open the Plugin Manager, click on the menu bar Plugins ▸ Manage and Install Plugins.



2. In the dialog that opens, write “GeoCoding” into the search box.
3. Click the Install Plugin button below the plugin information panel.

4. Select the Installed option in the Plugin Manager dialog.
5. Click in the box next to this plugin and check it to activate it.

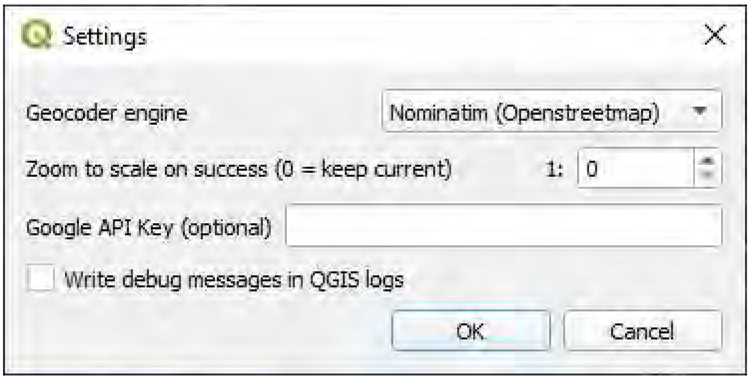
6. Click with the right button on the Toolbar and select “Plugins Toolbar”.



7. The Geocoding tool will apear on the Toolbar. 

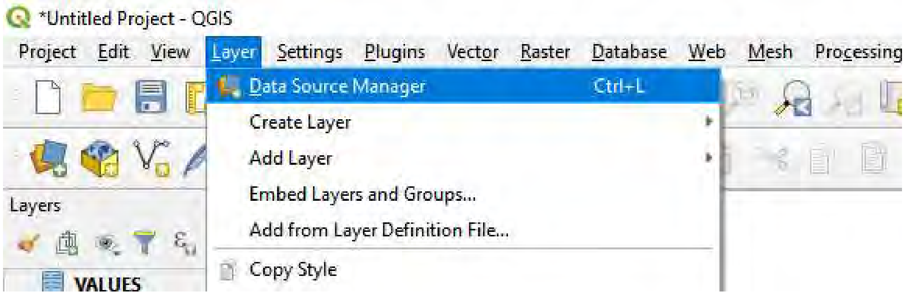
8. Click on the menu bar Plugins ▸ GeoCoding ▸ GeoCoding.

9. Select “Nominatim (Openstreetmap)” as geocoder engine.

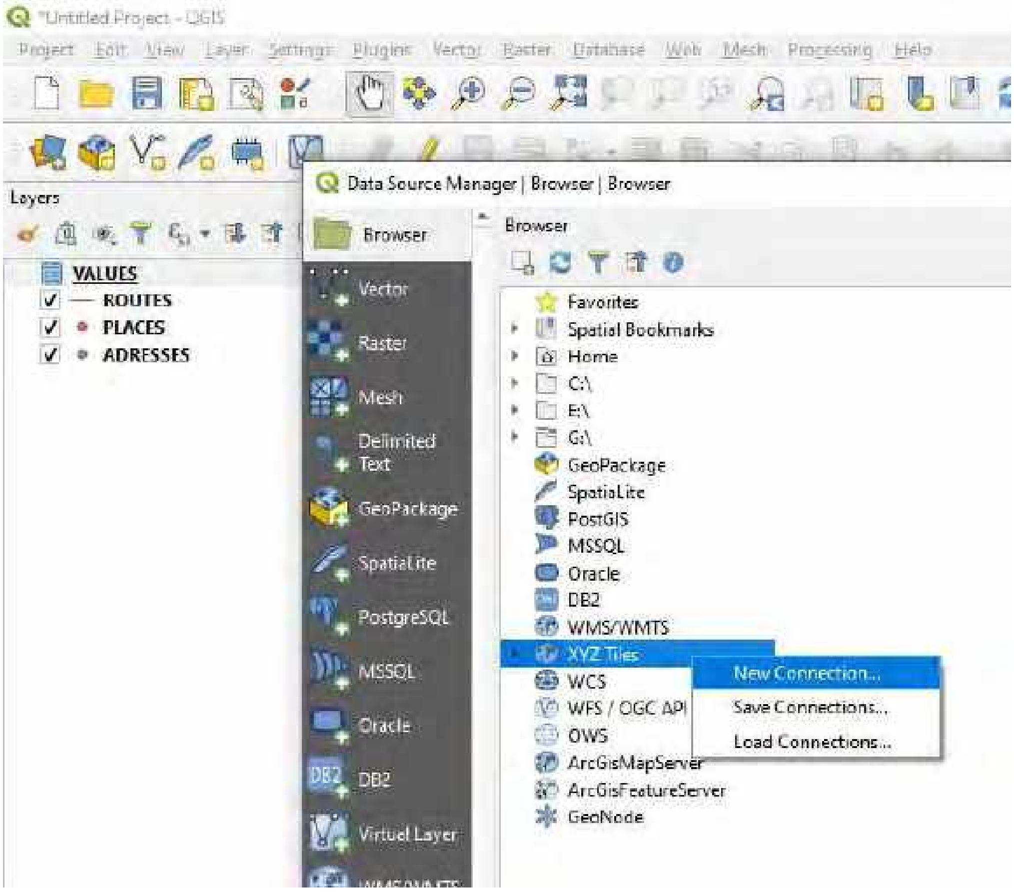


5.1.4. *Add Google and OpenStreet Maps as XYZ Tiles*

1. Click on the menu bar Layer ▸ Data Source Manager.

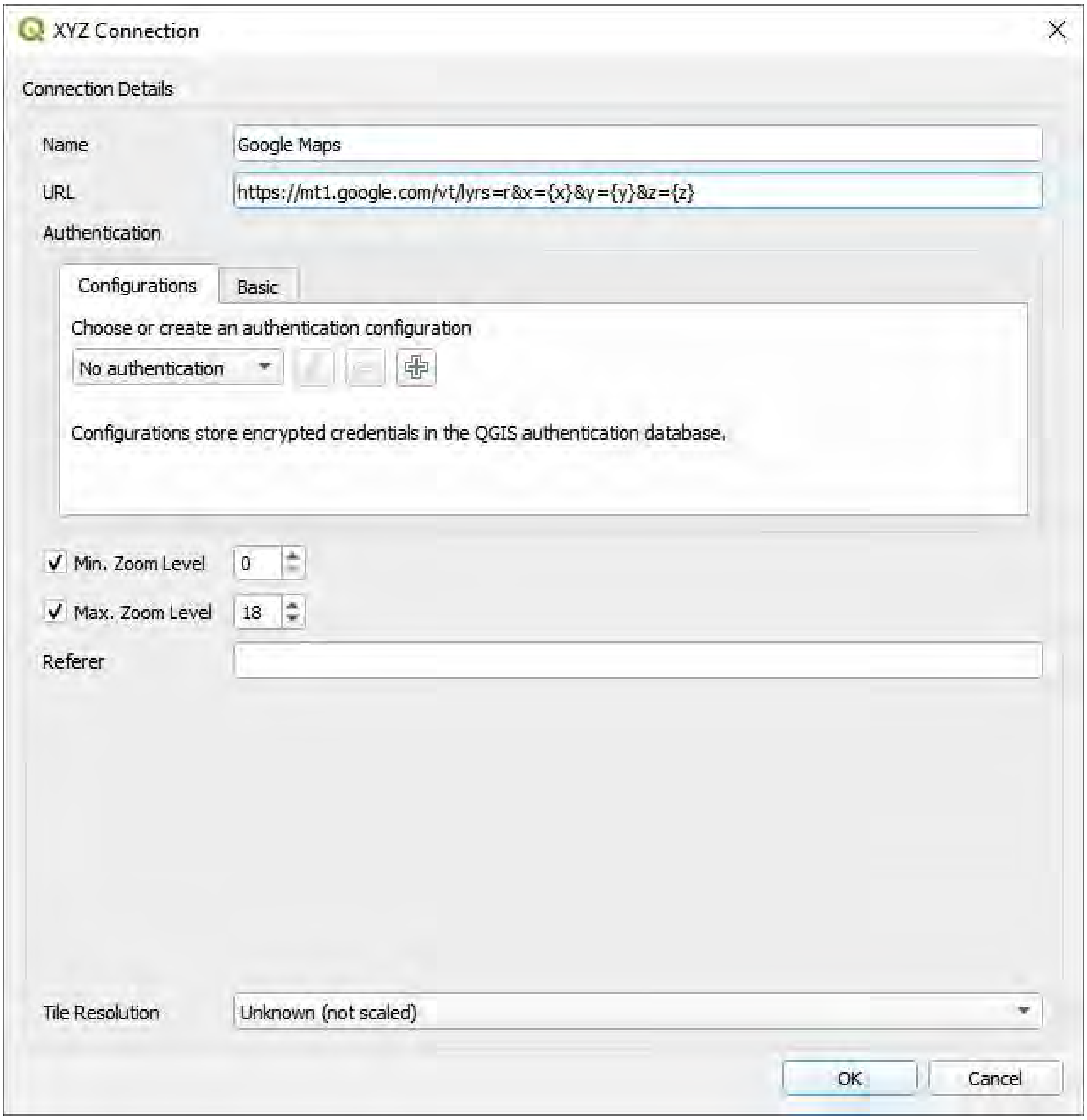


2. Make a new connection, with right click the XYZ Tiles.



3. Fill the name and URL boxes as detailed below:
    a. Google Maps: https://mt1.google.com/vt/lyrs=r&x={x}&y={y}&z={z}

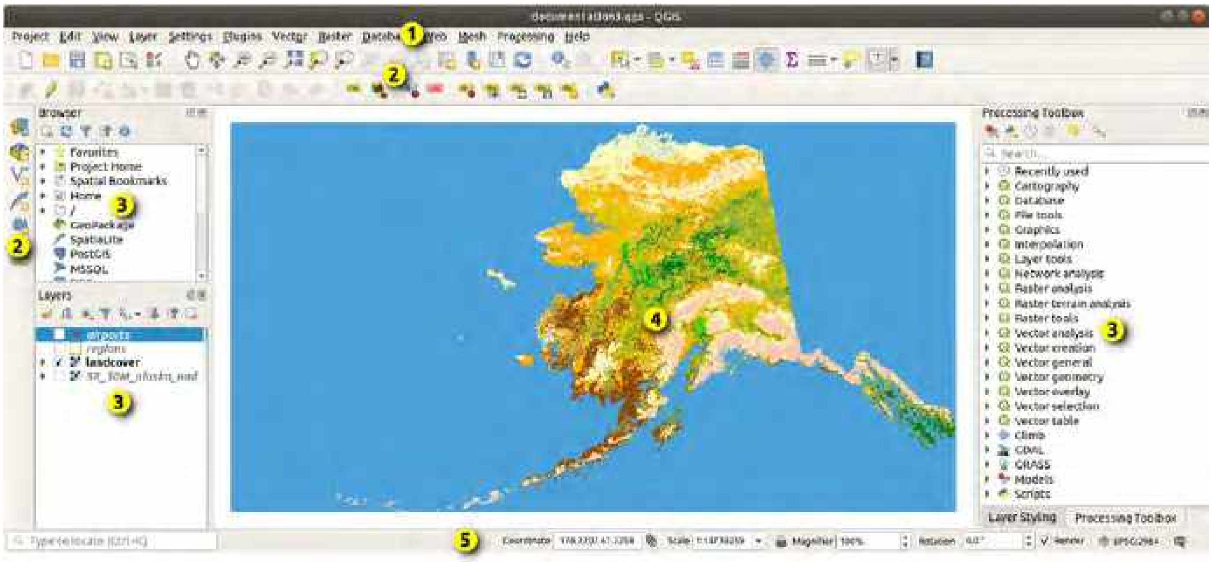
b. Google Satellite: http://www.google.cn/maps/vt?lyrs=s@189&gl=cn&x={x}&y={y}&z={z}
c. Google Satellite Hybrid: https://mt1.google.com/vt/lyrs=y&x={x}&y={y}&z={z}
d. Open Street Maps: https://tile.openstreetmap.org/{z}/{x}/{y}.png



5.2. Fast tutorial on QGIS

5.2.1. Graphical user interface

The QGIS graphical user interface (GUI) is shown in the figure below (the numbers 1 through 5 in yellow circles indicate important elements of the QGIS GUI, and are detailed below).



The main QGIS GUI (QGIS GUI with Alaska sample data) consists of five components / component types:

- 1 = Menu Bar
- 2 = Toolbars
- 3 = Panels
- 4 = Map View
- 5 = Status Bar

5.2.2. Exploring the map view

- it can be panned, shifting the display to another region of the map: this is performed using the Pan Map tool, the arrow keys, moving the mouse while any of the Space key, the middle mouse button or the mouse wheel is held down.

- it can be zoomed in and out, with the dedicated Zoom In and Zoom Out tools. This is also performed by rolling the wheel forward to zoom in and backwards to zoom out. The zoom is centered on the mouse cursor position.

- it can be zoomed to the full extent of loaded layers (Zoom Full), to a layer extent (Zoom to Layer) or to the extent of selected features (Zoom to Selection)

- you can navigate back/forward through canvas view history with the Zoom Last and Zoom Next buttons or using the back/forward mouse buttons.

5.3. Data to be geocoded

5.3.1. Point locations

We are going to geocode two kinds of point locations:

1) Home addresses
2) School address.

5.3.2. Commuting routes

We are going to geocode the common commuting routes between home and school, and school to home.

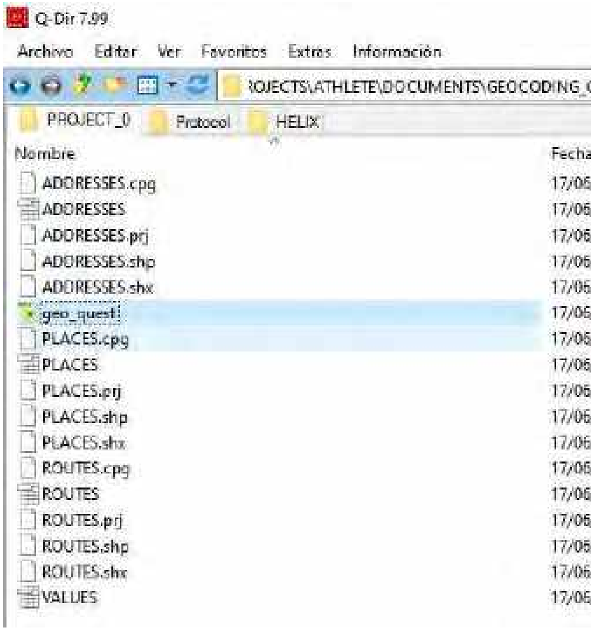
5.4. Start a new geocoding questionnaire

5.4.1. Create the participant's id folder questionnaire

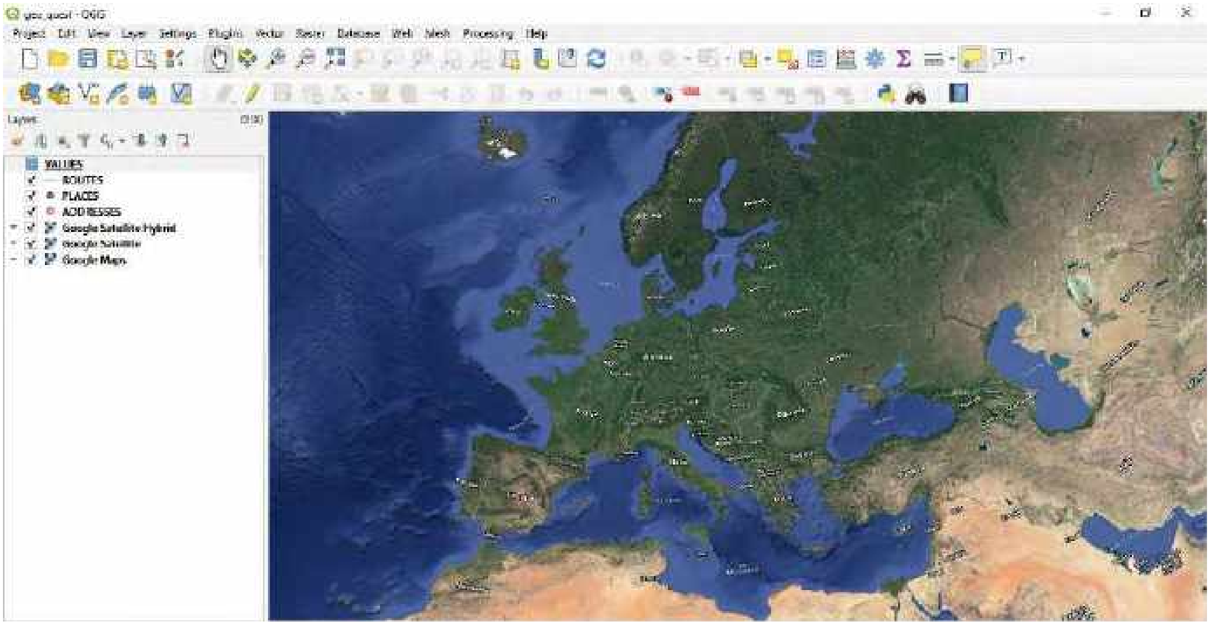
GEOCODING_QUESTIONNAIRE\PROJECT_0 folder is the template project to create each participant's questionnaire. It is very important to maintain an original copy of this directory without editing any of the files.

To start a new questionnaire, copy this folder and paste it changing the name of the folder: put participant's id as the name of the folder. Repeat the same procedure at the beginning of each questionnaire.

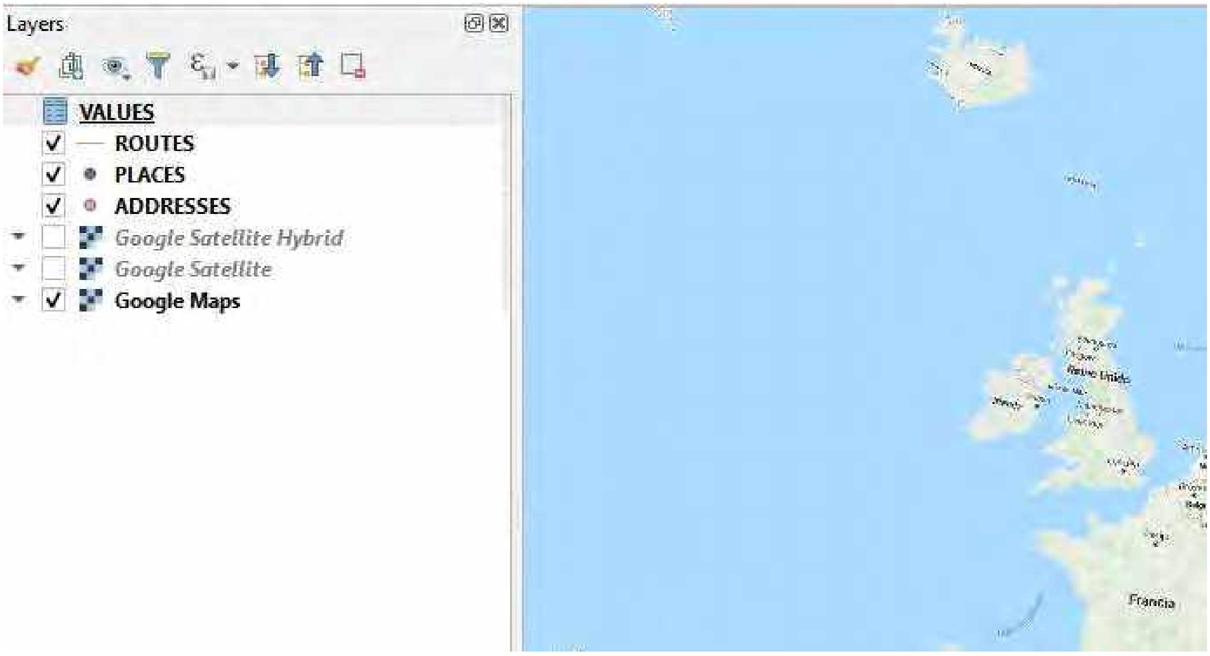
Open the specific project you will find in the new folder you have created: GEOCODING_QUESTIONNAIRE\xxxx\ geo_quest.qgs



A QGIS project will be opened:



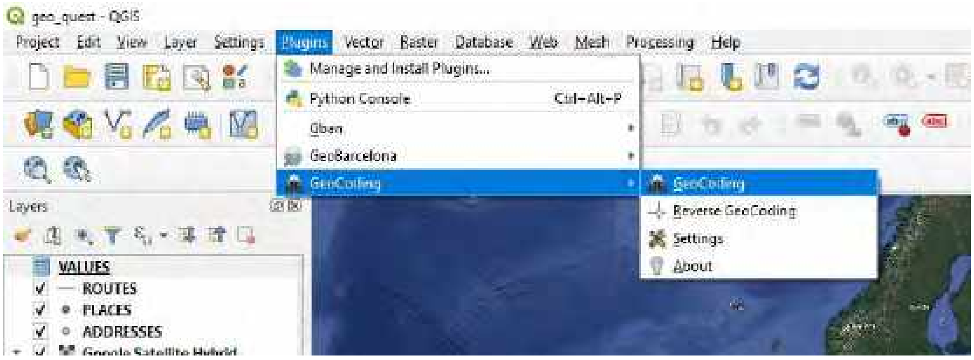
You can select/unselect google layers to see or not to see them.



5.4.2. How to geocode points

1. You are going to edit one layer to add new points:
    a. "ADDRESSES" (for home and school addresses)

2. Click on the menu bar Plugins ▸ GeoCoding ▸ GeoCoding.

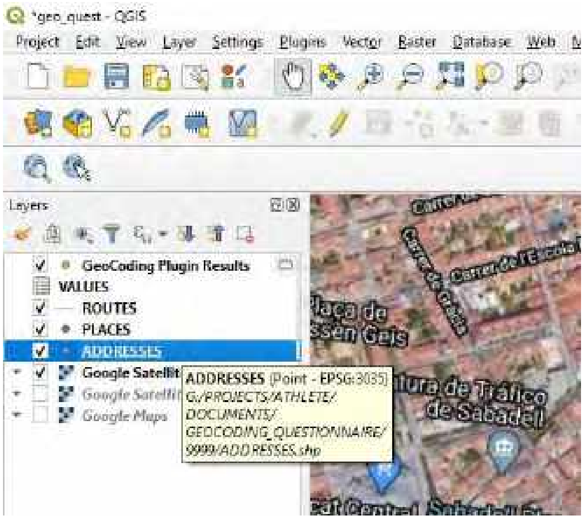


A new window will appear on your screen. You can move it wherever you want.

3. Write in the white space under "Find Address", the address of the child, school, or place, and click "OK".

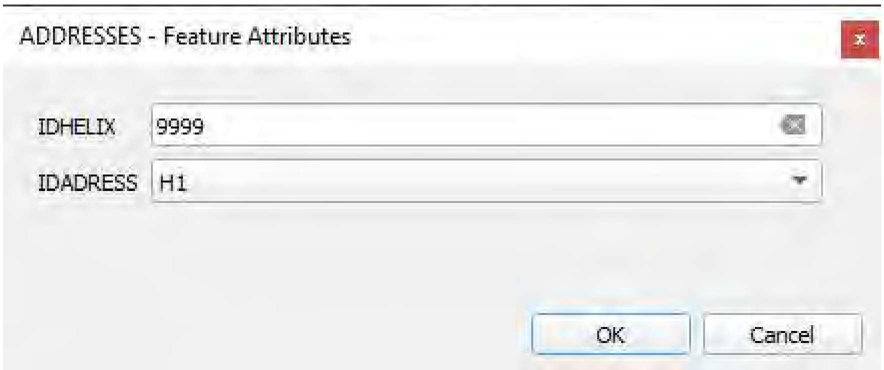
4. A point will appear on the map: <u>this point is not the address you are searching, it is drawn in the middle of the street you are searching</u>. So then, with the help of the participant, you should find the portal of the exact address you are searching on this street, and draw a point following the next instructions. If you don't find it, you can search it on https://www.google.es/maps.

5. Click with the left mouse button over the layer ("ADRESSES"). The layer will turn on blue.



6. In the main toolbar, click "Toggle editing" tool: . You will see a pen on the left of the layer: 

. This means that the layer is now editable (you can draw new features).
7. Select "add point feature" tool: 
8. Draw a new point over the exact address location clicking with the left button.
9. A new window will appear. It asks you for this new point attributes
    a. "ADDRESSES" layer:
        i. ID: It is the participant ID
        ii. IDADDRESS:
            1. Home address: H1, H2, H3.
            2. School address: S1.



10. Do the same for every point you draw.
11. When you have finished drawing all the points, in the main toolbar click "Toggle editing" tool: .
12. Save the changes.
13. To see the points you have drawn, click on left mouse button on the layer then on "Zoom Full" tool, in the main toolbar: 

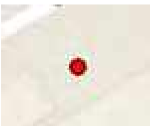
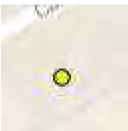
5.4.3. How to modify the attributes (if it is necessary)

Click on the layer with the left mouse button.

1. In the main toolbar, click “Toggle editing” tool: .
2. Click on “open attribute table” button in the main toolbar: 
3. Do the changes in the table.
4. Close table.
5. Click “Toggle editing” tool: .
6. Save the changes.

5.4.4. How to delete points (if it is necessary)

1. Click with the left mouse button the layer.
2. In the main toolbar, click “Toggle editing” tool: .
3. Click on “select features by area or single click” tool in the main toolbar. 
4. Select the point clicking on it (it will change colour to yellow). If you want to deselect click on the map.

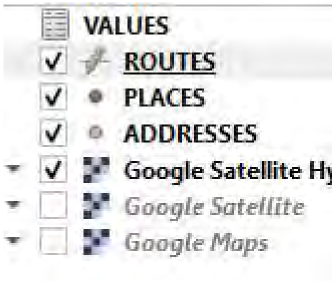
 

5. Click on “delete selected” button (all selected features will be deleted): 
6. Click “Toggle editing” tool: .
7. Save the changes.

5.4.5. How to geocode commuting routes

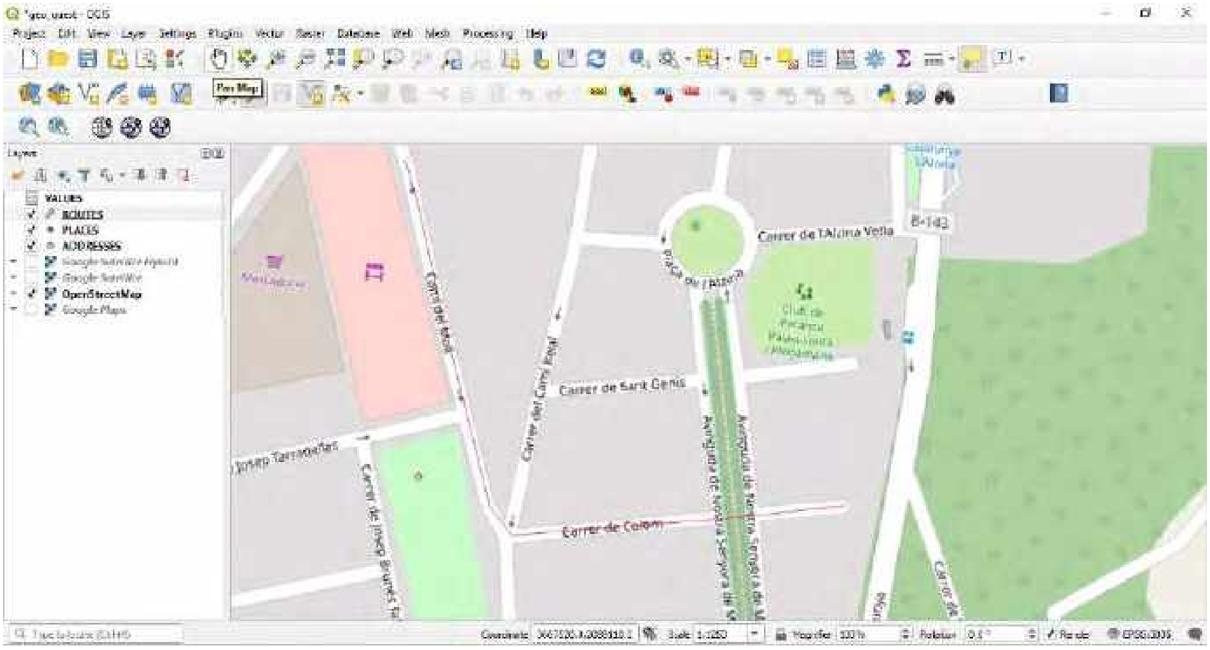
You will find a layer named “ROUTES”. You are going to edit this layer to add new routes.

1. Click over “ROUTES” with the left mouse button. This layer will turn on blue.
2. In the main toolbar, “Toggle editing” tool: .
3. You will see a pen on the left of the layer:

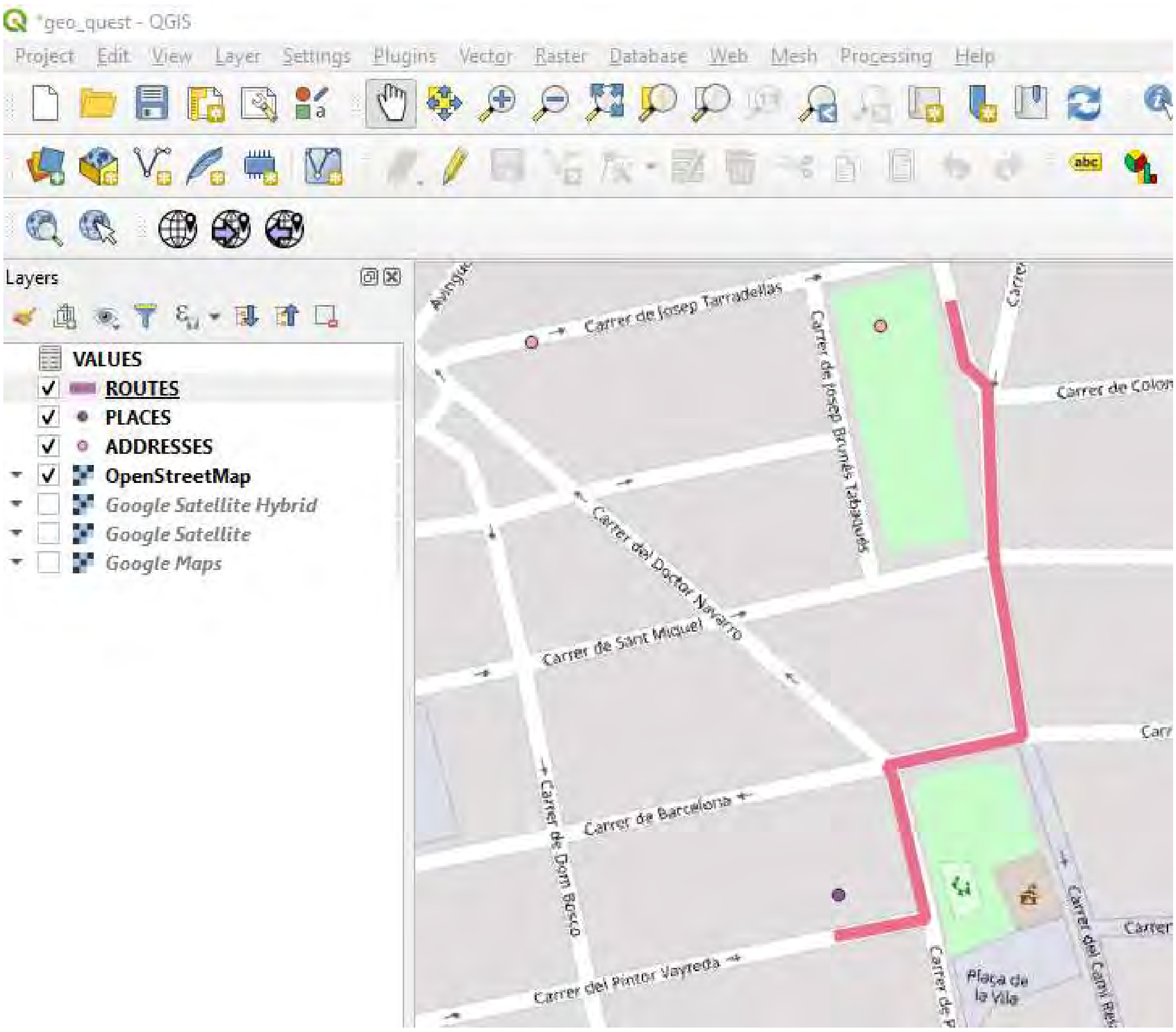


This means that “ROUTES” layer is now editable (you can draw new features).

4. Select the “Add line feature” button:  .
5. To start drawing the route left-click on your mouse at the starting point (one of the location point you have already drawn) and draw the route with your mouse left-clicking again to change directions. Click with the right button to finish.
6. If you are drawing a line and you have to continue drawing outside the map on your screen, click on “pan map”, keep pressing left-mouse bottom on the map and drive the mouse throughout the map. Select “Add feature” button and continue drawing the line.



7. Draw your route:



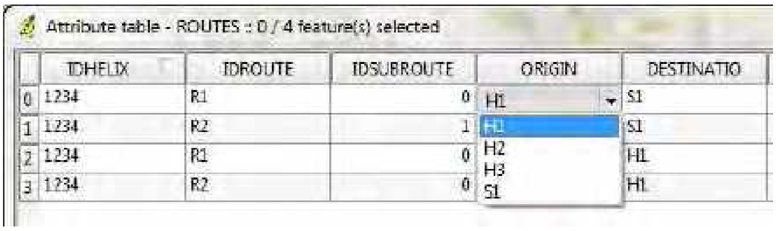
8. When the line is drawn, a new window will appear. It asks you for this new point attributes: ID, ID ROUTE, ID SUBROUTE, ORIGIN, DESTINATION, DIRECT TRIP and OBSERVATIONS. Fill the attributes as detailed below:
    a. ID: participant ID
    b. IDROUTE: R1, R2, R3 and so on.
    c. IDSUBROUTE:
        i. If you have only 1 transport mode: 0
        ii. If you have more than 1 transport mode: in that cases the IDROUTE will be the same but the IDSUBROUTE will be 1, 2, 3 and so on.
    d. ORIGIN: ID of addresses that corresponds to the origin (home: H1, H2; school: S1).
    e. DESTINATION: ID of addresses that corresponds to the destination (home: H1, H2, and; school: S1,).
    f. DAYS PER WEEK: number of days per week this route is done (the field can accept decimal numbers).
    g. DIRECT TRIP: Is the child doing the commuting route from home to school directly? Answer yes or no (not directly means that the child makes a stop in the middle of the route to go grandparents' house, take breakfast, do any activity like sports, goes to the park, etc.).

h. OBSERVATIONS: Write here any other information you consider relevant.

9. You have to do the same for every route you draw.
10. When you have finished drawing all the routes, in the main toolbar click "Toggle editing" tool: .
11. Save the changes to layer "ROUTES".
12. To see the routes you have drawn, click on left mouse button on the layer "ROUTES" then on "Zoom Full" tool, in the main toolbar: .

5.4.6. How to modify the attributes (if it is necessary)

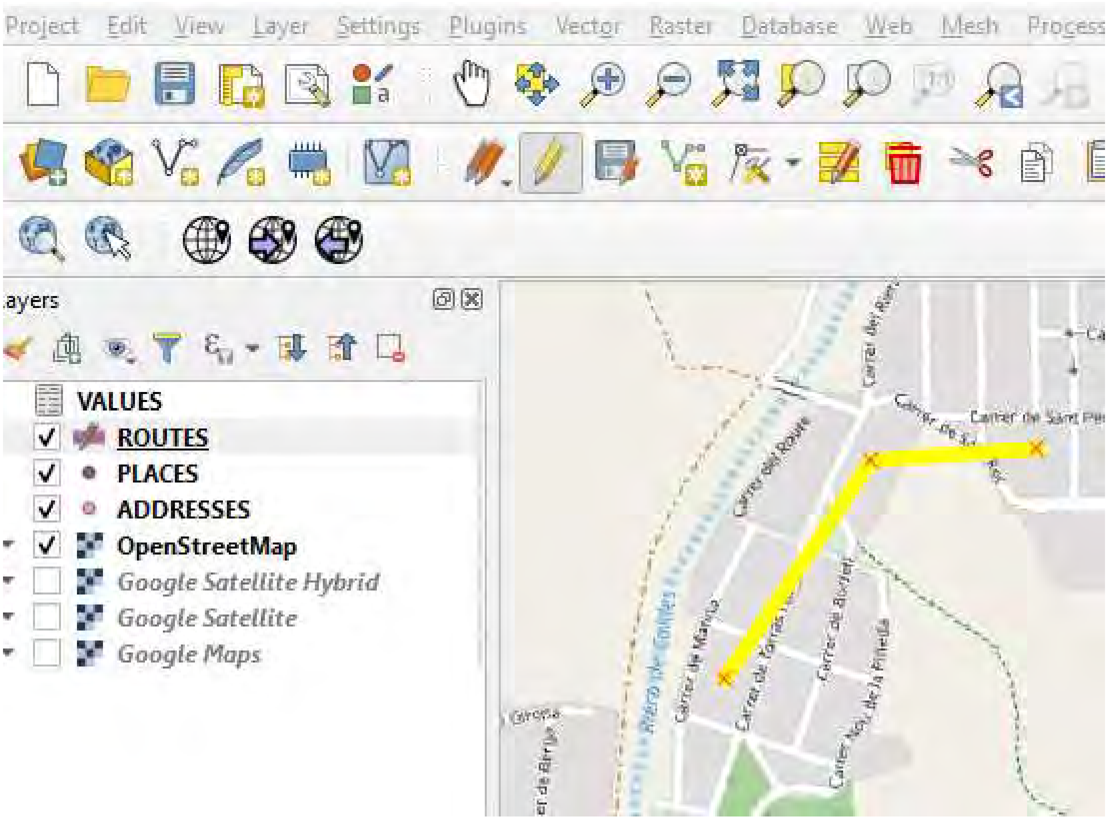
1. Click with the left mouse button the layer.
2. In the main toolbar, click "Toggle editing" tool: .
3. Click on "open attribute table" button in the main toolbar: 



4. Do the changes.
5. Close table.
6. Click "Toggle editing" tool: .
7. Save the changes.

5.4.7. How to delete lines (if it is necessary)

1. Click with the left mouse button the layer.
2. In the main toolbar, click “Toggle editing” tool: .
3. Click on “select features by area or single click” tool in the main toolbar. 
4. Select the line clicking on it (it will change colour to yellow). If you want to deselect it click on the map.



8. Click on “delete selected” button (all selected features will be deleted): 
9. Click “Toggle editing” tool: .
10. Save the changes.

11. QUALITY CONTROL

When ISGLOBAL will receive all geocoding questionnaires, there will be a quality control on the data received. It will be checked:

1. If there is NA in any column,

2. number of ids, number of addresses per id,
3. if the sum of number of days is > 5,
4. if hs_origin != hs_destination
5. if there are duplicated routes

If any inconsistence is detected, we will ask to cohort to check them.

12. REFERENCES

- QGIS Development Team, <2020>. QGIS Geographic Information System. Open Source Geospatial Foundation Project. http://qgis.osgeo.org
- QGIS Development Team, <2020>. QGIS <3.12.3 > Geographic Information System User Guide. Open Source Geospatial Foundation Project. Electronic document: http://download.osgeo.org/qgis/doc/manual/<DOCUMENT>
- Python GeoCoding Plugin; Author: Alessandro Pasotti; info@itopen.it; www.itopen.it.