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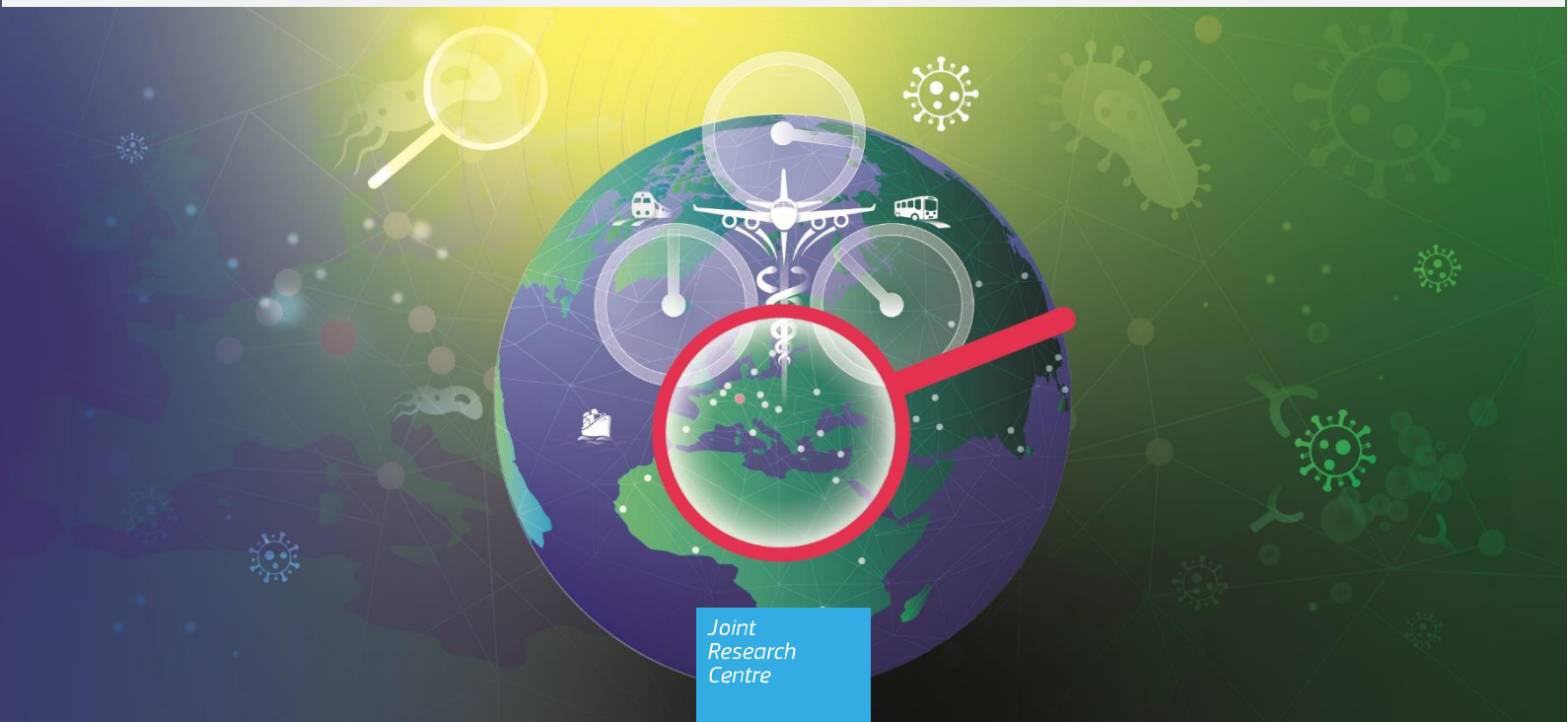

Contact information
Name: Bernd Manfred Gawlik
Address: Via Enrico Fermi 2749, I-21027 Ispra/Italy
Email: bernd.gawlik@ec.europa.eu
Tel.: +39 0332 78 9487

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Integrated environmental and clinical surveillance for the prevention of acute respiratory infections in closed settings and vulnerable communities: school, prison and nursing home (Stell-ARI Project)

Annalaura Carducci [1] (annalaura.carducci@unipi.it), Laura Carrozzi [2], Laura Baglietto [3], Francesco Pistelli [2], Marco Verani [1], Marco Fornili [3], Lara Tavoschi [4], Ileana Federigi [1], Tommaso Lomonaco [5], Antonello Agostini [4], Guglielmo Arzilli [4], Nebiyu Tariku Atomsa [1], Giulia Lauretani [1], Claudia Meschi [2], Alessandra Pagani [1], Davide Petri [3], Daniela Paolotti [6], Caterina Rizzo [4]

[1] Department of Biology, University of Pisa, Pisa, Italy [2] Department of surgical, medical and molecular pathology and critical care medicine, University of Pisa, Pisa, Italy [3] University of Pisa, Department of clinical and Experimental Medicine, Pisa, Italy [4] Department of Translational Research and New technologies in Medicine and Surgery, University of Pisa, Pisa, Italy [5] Department of Chemistry and Industrial Chemistry, University of Pisa, Pisa, Italy [6] ISI Foundation, Turin, Italy

Background

Wastewater Based Epidemiology (WBE) has been demonstrated as a valuable tool for the early warning in SARS-CoV-2 epidemic in small communities, mainly university campuses and nursing homes (Davó et al. 2021), while fewer information is reported about primary schools (Kapoor et al. 2022) and very few on prisons (Hassard et al. 2022). WBE could also be used for monitoring other acute respiratory infections (ARIs), such as Influenza and Respiratory Syncytial Virus, in small communities where they can represent relevant threats.

For public health purposes, a surveillance system in small communities should be able to foresee with a sufficient precision the onset of an outbreak to enable the timely adoption or reinforcement of preventive measures but should also be sustainable (Figure 1). To this aim, continuous microbial risk assessment should be implemented to identify areas and situations requiring preventive measures. Moreover, an early warning system should be able to detect the initial introduction of the infection into the community, prompting the reinforcement of preventive measures. Therefore, clinical surveillance will be the last action after the onset of an epidemic, allowing for the prevention of the outbreak diffusion. Usually, this last is the only point of observation, thus hampering a more effective prevention.

Figure 1. Surveillance pathway for infectious diseases. QMRA = Quantitative Microbial Risk Assessment, WBE = Wastewater-Based Epidemiology

Objectives

The project entitled "*Environmental integrated surveillance of acute respiratory illnesses (ARI) in closed environments and vulnerable communities*" (acronym: Stell-ARI) funded by PNRR (National Recovery and Resilience Plan) by the Italian Ministry of University and Research, has the general objective of integrating clinical, behavioural, and environmental data to establish and validate a predictive model and risk assessment tool for the early warning and risk management of viral ARIs in closed and vulnerable communities. In this framework, more specific objectives include: (i) monitoring environmental data for risk assessment and early warning, (ii) collect clinical ARIs data, (iii) integrating clinical and environmental data to develop models of Quantitative Microbial Risk Assessment and early warning.

Study Settings

The study includes three settings with specific features as reported in the Table 1

Table 1. Study settings and their specific features

Study setting	Selected pilot	Features
School	*«L. Gereschi» of Pisa*	- Crowded structures - Lower acquired immunity -Higher contact among children
Prison	*Prison of Lucca*	- Crowded setting - Poor sanitary conditions - High-risk factors (i.e., substance use and drugs) - Poor ventilation
Nursing Home	*«Le Sorgenti» of Pisa*	- Use of common spaces - Advanced age - High comorbidity

Project Workflow

After receiving authorization from the Ethical Committee, the study protocol was registered on the European Union electronic Register of Post-Authorisation Studies (EU PAS Register) with the protocol registration number EUPAS106190. In each setting, an integrated clinical and environmental-based surveillance is carried out, coupled with analytical methods for environmental matrices. The workflow can be summarized as follows:

(32) **Basal information on participants and environment**, that are acquired through questionnaires administrated at the beginning of the study, both to participants to investigate behaviors and living conditions that could affect health toward ARIs (Charlson et al., 2008) and to managers of each setting to understand the environmental features of the buildings.

(33) **Clinical and environmental surveys**. Clinical survey involves participants with respiratory symptoms who are asked to fill a clinical questionnaire and to provide a nasal swab analyzed for respiratory viruses. The environmental survey includes weekly sewage monitoring and monthly air and surface monitoring.

(34) **Data analysis and models**. Through data analysis the most significant variables for the implementation of risk assessment and early warning systems in a sustainable way, will be selected. Data from air and surface monitoring will be used for QMRA models, while data from clinical surveillance and sewage monitoring will be used for early warning models. Moreover, the output of QMRA and early warning can be coupled to improve the effectiveness of risk management of viral ARIs in closed and vulnerable communities prior to the onset of an outbreak.

The study started in December 2022, and it is ongoing, as detailed below:

1. **Preparatory actions** (completed), including acquisition of personnel, protocol and workflow, questionnaires, analytical methods, sampling strategy, data base, ethical committee approval, registration of the protocol;
2. **Enrollment activities** (completed); the three settings (school, nursing home, prison) have been enrolled with agreements for collaboration.
3. **Basal survey** (in progress) questionnaires on basal clinical and environmental information are being administered and preliminary exploratory sampling has been conducted to identify the sampling points.

In 2024, follow up activities will be carried out, including both people (case detection, questionnaires, and swabs) and the environment (air, surface and wastewater monitoring). In 2025, data analysis, modelling (QMRA and Early Warning) and reporting will be carried out, together with the dissemination of results.

Material and Methods for Environmental Monitoring

In each setting, environmental monitoring includes three different matrices: wastewaters (immediately at the exit of each building, before flowing into the public sewer network), and air and surfaces.

The target viruses are: Human Adenovirus (HAdV; chosen as the index pathogen), Influenza Virus A and B (IVA and IVB), SARS-CoV-2, Respiratory Syncytial Virus Type A and Type B (RSVA and RSVB). These viruses are searched in every matrix, with specific sampling procedures (see registered protocol) followed by biomolecular methods. Other microbiological parameters include the total bacterial count at 37°C, *Escherichia coli* and *St. aureus*, which are only searched in air and on surfaces. Moreover, air samples are tested also for chemical parameters, including humidity, CO2 levels, particular matter (PM2.5), and total volatile organic compounds (VOCs). To identify highly contaminated areas, a preliminary monitoring campaign has been carried out through passive bioaerosol sampling using settling agar plates. In each setting, environmental monitoring encompasses three different matrices: wastewaters (immediately at the exit of each building, before flowing into the public sewer network), and air and surfaces.

Previous and Preliminary Results

WBE monitoring in Pisa: In the study area of Pisa (Tuscany, Italy), a WBE monitoring has been carried out since 2021 for SARS-CoV-2 and HAdV, and since 2022 for RSA and IV. In parallel, clinical data reported in the same area to the regional surveillance system were available only for SARS-CoV-2. Limited clinical data for RSV and IV were reported at a national level by the Italian National Clinical Surveillance on Respiratory viruses (RespiVirNet; *https://www.epicentro.iss.it/influenza/respivirnet*). For SARS-CoV-2, correlations between WBE and cases were globally significant, with differences according to phases and periods (Carducci et al., 2023). The HAdV occurrence in sewages was very high (80.2%), with seasonal differences probably due to the circulation of enteric strains, but the lack of epidemiological data hampers the integration between environmental and clinical data. Regarding RSV, it was detected in only 36.9% of sewage samples during the period corresponding to the peak in RespiVirNet. Influenza viruses were never detected, probably due to a method failure.

Exploratory sampling in study settings: The overall microbial contamination of various areas in each study setting has been categorized on the basis of percentile classification, as detailed in Figure 2. From these results, the most contaminated areas in each setting have been chosen for air and surface monitoring.

Figure 2. Results of the preliminary screening of air contamination in the three settings. The contamination level is represented by different colors associated to each sampling areas (green = very low, yellow = low, orange = moderate, red = high, dark red = very high).

Number of sampling areas	School	Prison	Nursing home
1	Teacher room	Administrative office	Double guest room
2	Corridor (ground floor)	Infirmary	Staff room (shelf)
3	Canteen (entrance)	Psychologist room (baseline)	Dining room (floor)
4	Canteen (near hydrant)	Visiting room	Dining room (shelf)
5	Audiovisual room	Officers' canteen	Infirmary
6	Lumber room (baseline)	Corridor (first floor)	Living room (window)
7	Corridor (first floor)	Indoor recreational room for prisoner	Living room (shelf)
8	Classroom "Ranieri"	Officers' room	Reception (desk)
9	School gym	Corridor n.1 (second floor)	Reception (entrance)
10	Classroom "Galilei"	Corridor n.1AT (second floor)	Lumber room (baseline)

Final Comments

Although the proposed approach to the surveillance of ARIs in close communities is innovative and promising, given the complexity of the study and the large number of variables involved, problems can be expected, with:

(35) QMRA: low sensitivity of viral detection in air and on surfaces; difficulties in using indicators for this purpose due to the lack of correlation; scarcity of dose-response curves;
(36) Wastewater based surveillance: the access to an easy discharge point is sometimes impossible; a choice among composite, grab or passive samples is needed; possible method failures for some viruses;
(37) Clinical Surveillance: difficult participation of people (mainly parents of schoolchildren).

Overcoming these difficulties could allow for the development and implementation of an integrated system whose application would be very efficient for infection control in close communities.

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Network of Collaboration: University of Pisa Departments: Biology, Surgical, Medical and molecular pathology and critical care medicine, Translational Research and New technologies in Medicine and Surgery, Clinical and Experimental Medicine, Clinical and Experimental Medicine. Nursing Home "Le Sorgenti", Pisa. Primary School "L.Gereschi", Pisa. Prison of Lucca. ISI Foundation, Turin. Acque SpA, Pisa

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