

Preliminary results of the Eucare school studies and SARS-CoV-2 trends in Italy, Germany and Portugal and school opening during the Omicron variant

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BACKGROUND

As part of the global reaction to stop the spread of SARS-CoV-2, primary and secondary schools were closed to on-site instruction in many countries. Contradictory results were reported on the role of school closure/reopening on the SARS-CoV-2 transmission rate.

The Lolli-Methode, a non-invasive molecular salivary test developed by the Institute of Virology at UniKoeln and based on pool testing, can be a useful epidemiological surveillance tool to control the spread of the infection in schools and support school opening.

We also investigated the impact of school reopening on SARS-CoV-2 transmission in Italy, Germany and Portugal in autumn 2022, when the Omicron variant was prevalent and limited preventive measures were implemented in schools.

The study was conducted in the frame of the international collaboration on the EuCARE project (<https://eucareresearch.eu/>), funded by the European Union.

The EuCARE school studies

METHODS

The **EuCARE** school study designs:

- a **cluster randomized trial**, aimed to determine if the use of the Lolli-Methode is useful to support schools opening
- A **prospective cohort study** to investigate impact of preventive measures adopted in class.

Questionnaires covering ongoing mitigation measures, psychological impact, and other health and socio-economic information will be filled from children, parents, schoolteachers, and principals.

We will also estimate the prevalence of SARS-CoV-2 in schools, frequencies and size of clusters and attack rates, to compare the effectiveness of the different preventive measures adopted and to evaluate their psychological impact in students and teachers [Raimondi, S. et al. BMC Infect Dis 23, 1, 2023].

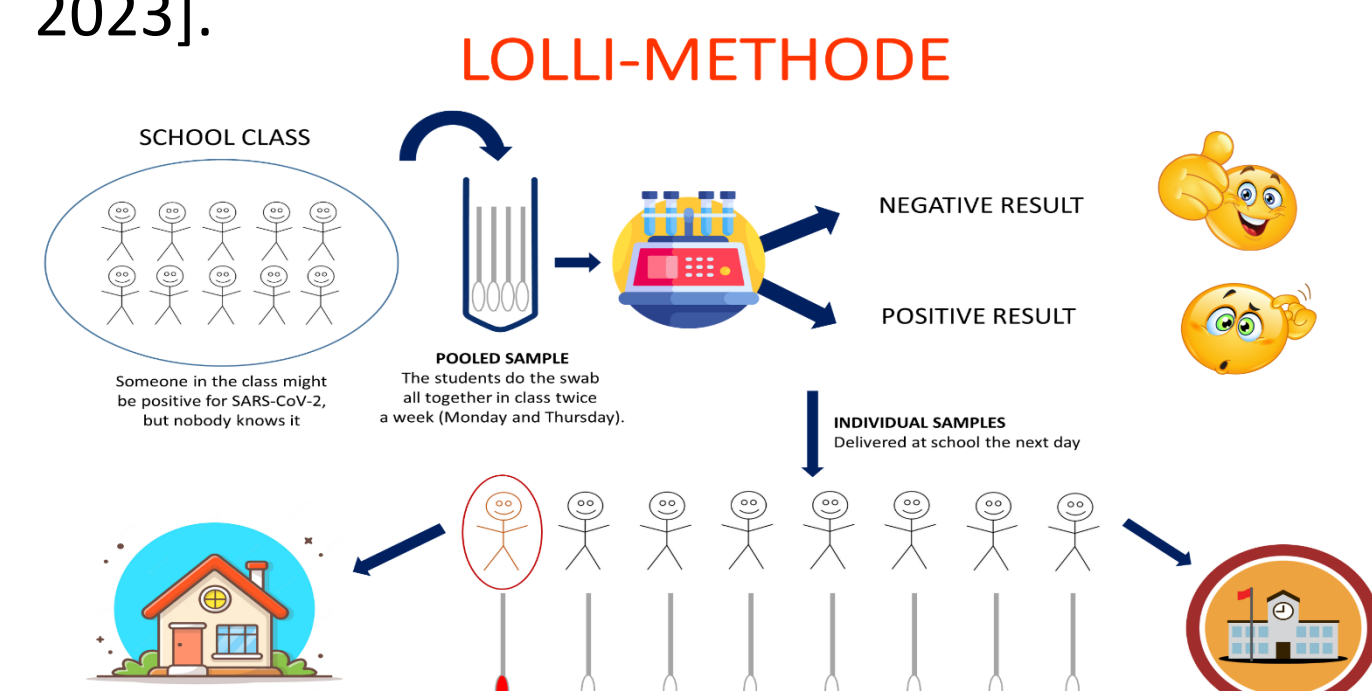


Figure 2. Schema showing the workflow of the Lolli-Methode in a school class.

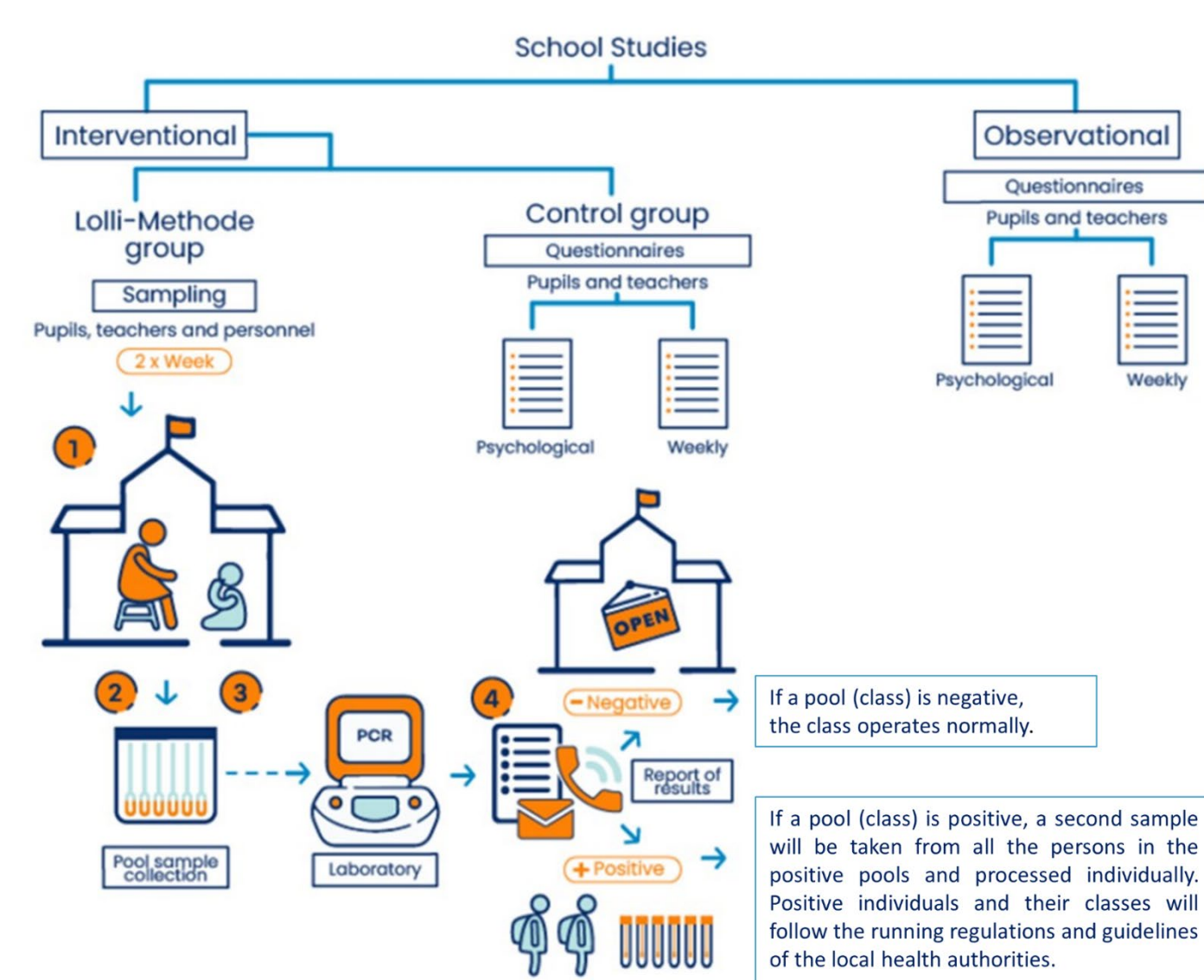


Figure 1. Flow chart of the study designs of the two EuCARE school studies.

The **Lolli-Methode** [Dewald, F. et al. Nat Commun 13, 3640, 2022] is a strategy for epidemiological surveillance and early intervention aiming at SARS-CoV-2 outbreaks' reduction in schools, relying on polymerase-chain-reaction analysis of saliva samples in two steps: on **pooled samples** and then on **individual samples** from positive pooled cases.

RESULTS

Table 1. Enrollment in the Randomized Trial and the observational cohort study in Italy by January 2023

	Total	N=1453	%
Types of subjects	Students	1094	75.3
	Teachers	253	17.4
	Family members	83	5.7
	Non-teaching staff	23	1.6
Study/arms	Observational study	326	22.4
	RT: Lolli arm	612	42.1
	RT: Standard of Care (SoC) arm	515	35.4
Center	North of Italy	532	36.6
	South of Italy	921	63.4

By the end of January 2023, in Italy we enrolled **1453 subjects**: 1127 in the randomized trial and 326 in the observational cohort study. 37% of the participants were from the North of Italy, 63% from the South.

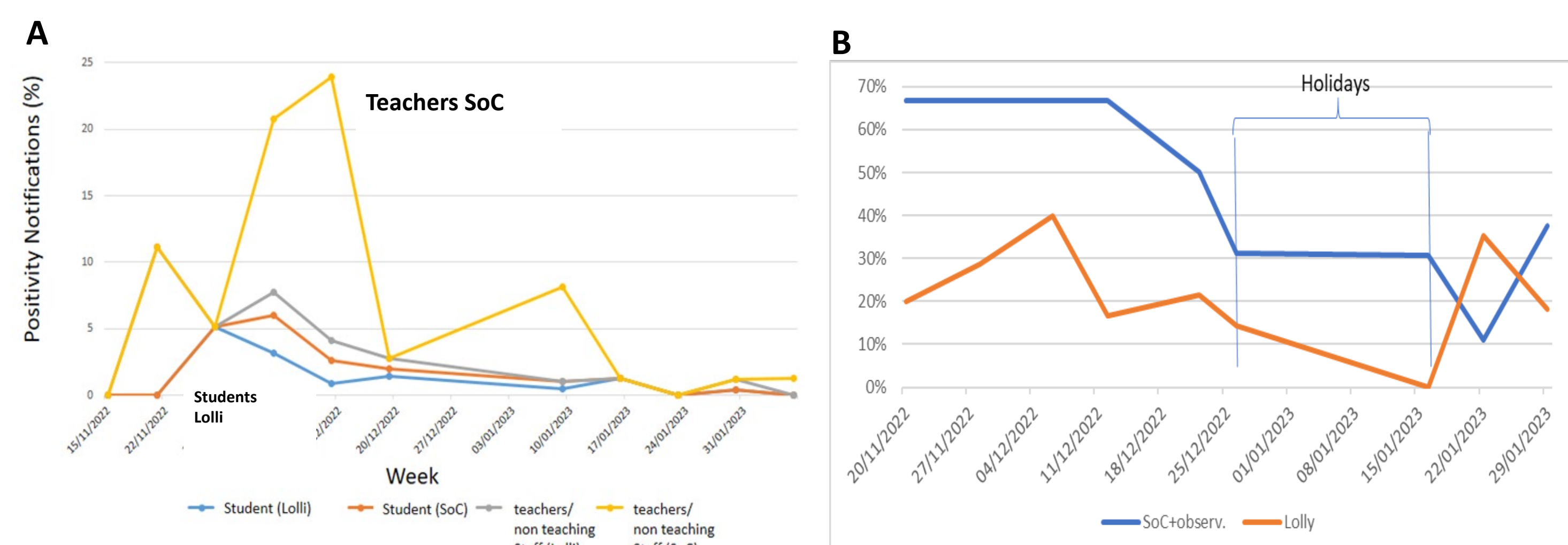


Figure 3. In A, positivity notifications (%) in the two groups (Lolli and SoC) over time between students and teachers/non-teaching staff. In B, rates of symptoms per week in families. Data from the randomized trial and from the observational study. SoC=Standard of Care.

Looking at trends in time of positive notifications, we found greater positive rates in the Standard-of-Care (SoC) trial arm for teachers and lower rates in the Lolli arm in students. Overall rates of symptoms per week were significantly lower in the Lolli arm: 47% for the SoC arm versus 23% for the Lolli arm ($p=0.009$). No differences were observed between groups regarding adopted preventive measures, except for the use of ventilation and opening of windows which were found significantly less frequent in the Lolli arm ($p=0.02$).

SARS-CoV-2 trends in Italy, Germany and Portugal during school opening in autumn 2022

METHODS

- We used the **case reproduction number (R_c)** calculated with the time parametrization of Omicron to investigate the potential impact of school reopening during autumn 2022 on SARS-CoV-2 transmission in Italy, Germany and Portugal.
- Data from regions/states reopening schools on the same day were pooled, and R_c curves were compared across age groups.
- For Germany and Italy, **staggered difference-in-differences (DID)** analysis was employed to explore the causal relationship between school reopening and R_c changes, accounting for varying reopening dates.
- In Portugal, **interrupted time series analysis (ITS)** was used due to simultaneous school openings.
- Multivariable models were adopted to adjust for confounders.

RESULTS

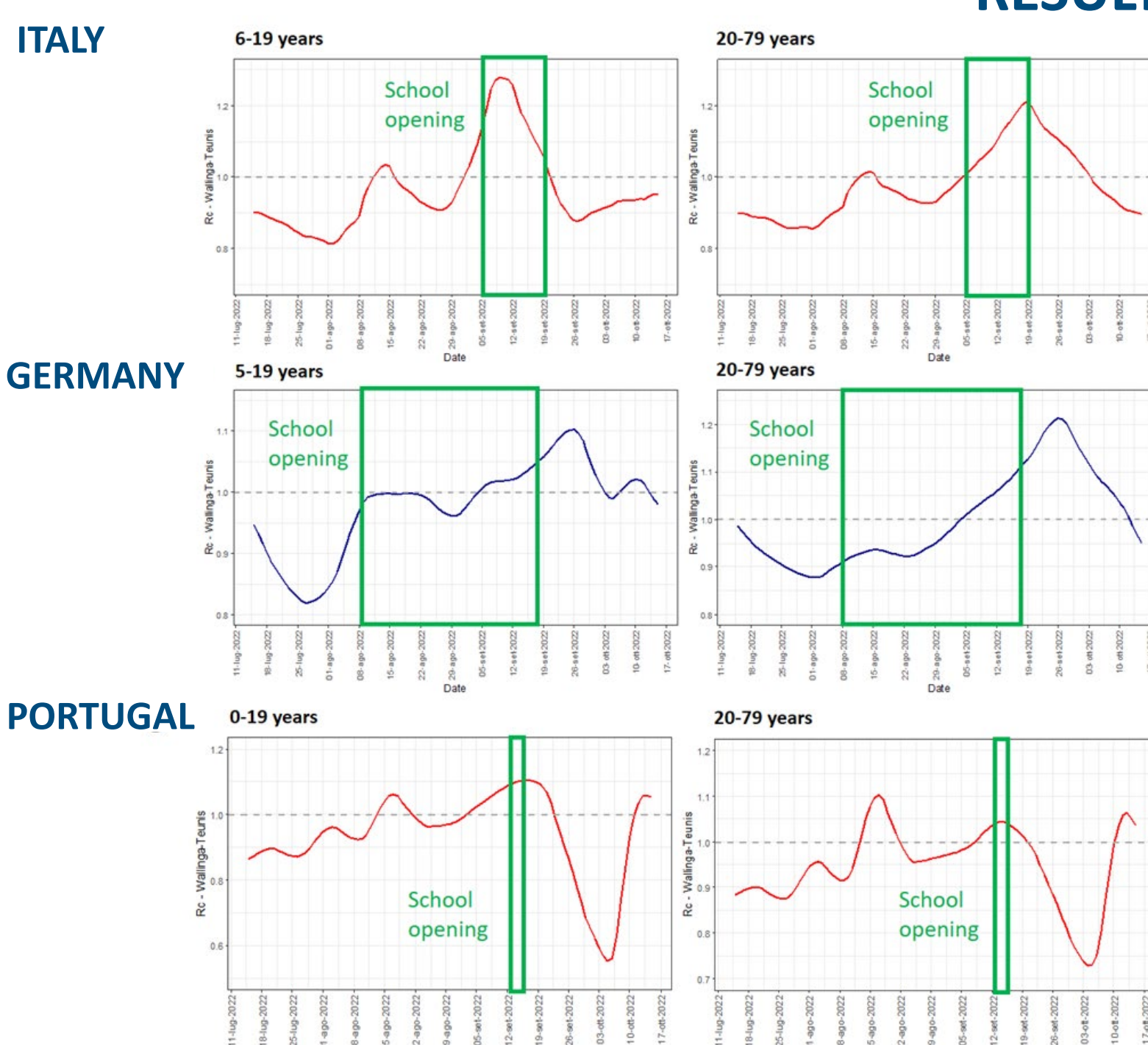
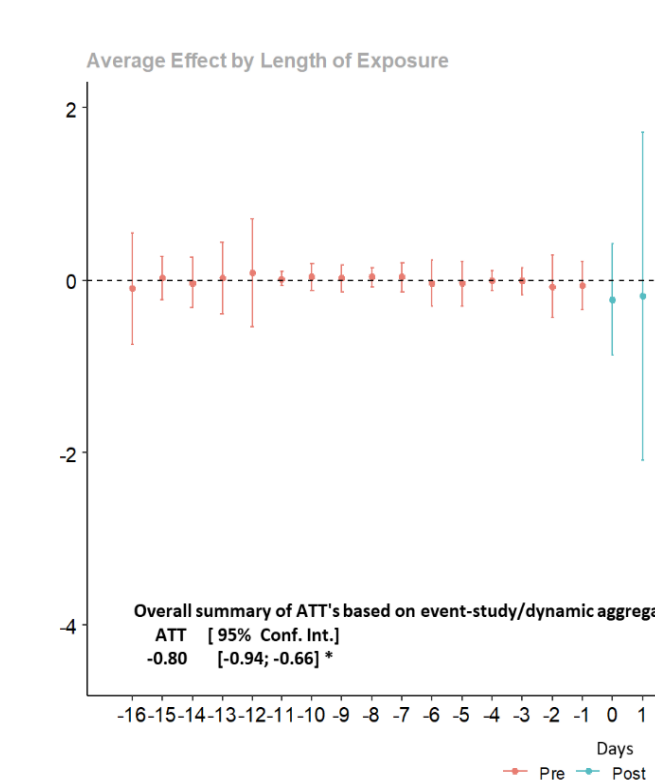


Figure 4. Curves of R_c estimates by population (student population and adult population) in Italy, Germany and Portugal from July 15th, 2022 and October 15th, 2022.

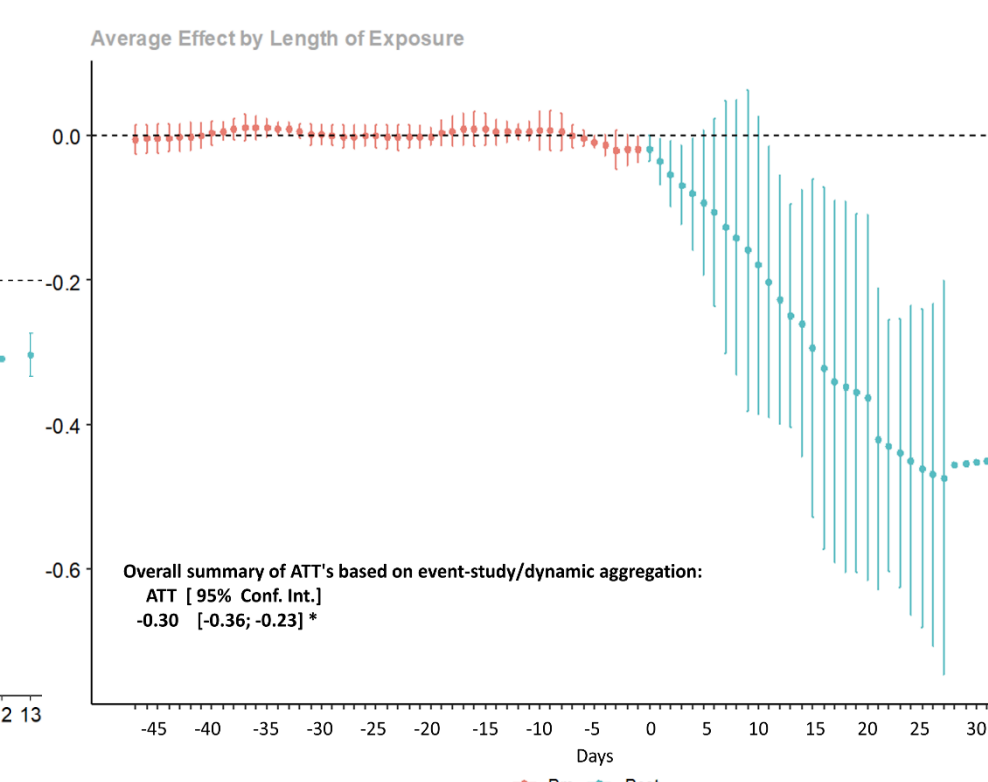
ITALY – Staggered DID model

A. 6-19 YEARS OLD



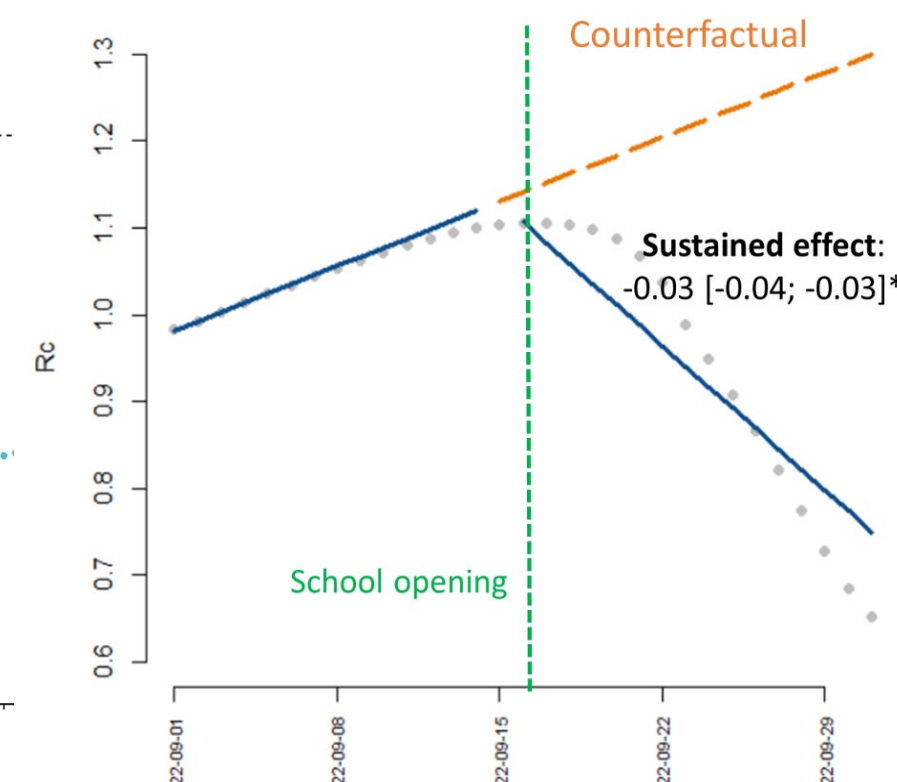
GERMANY – Staggered DID model

C. 5-19 YEARS

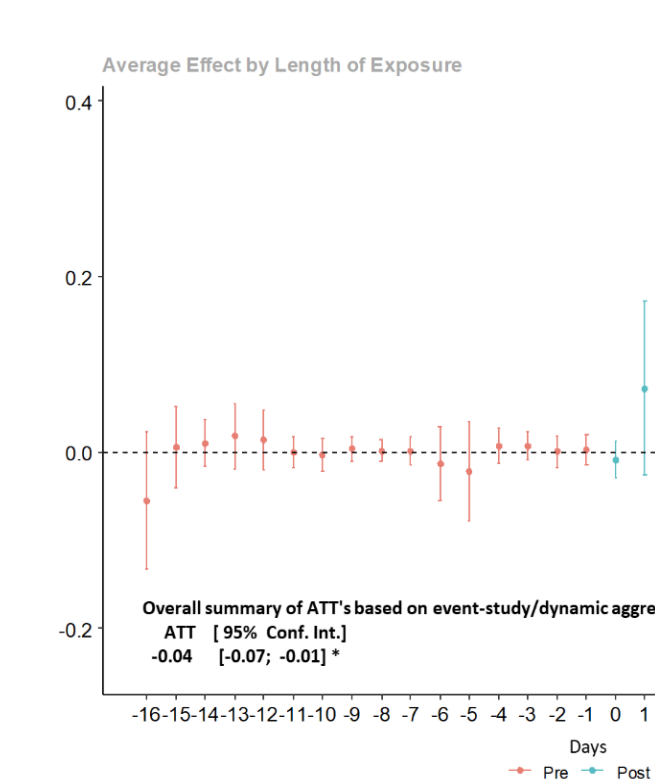


PORTUGAL – ITS model

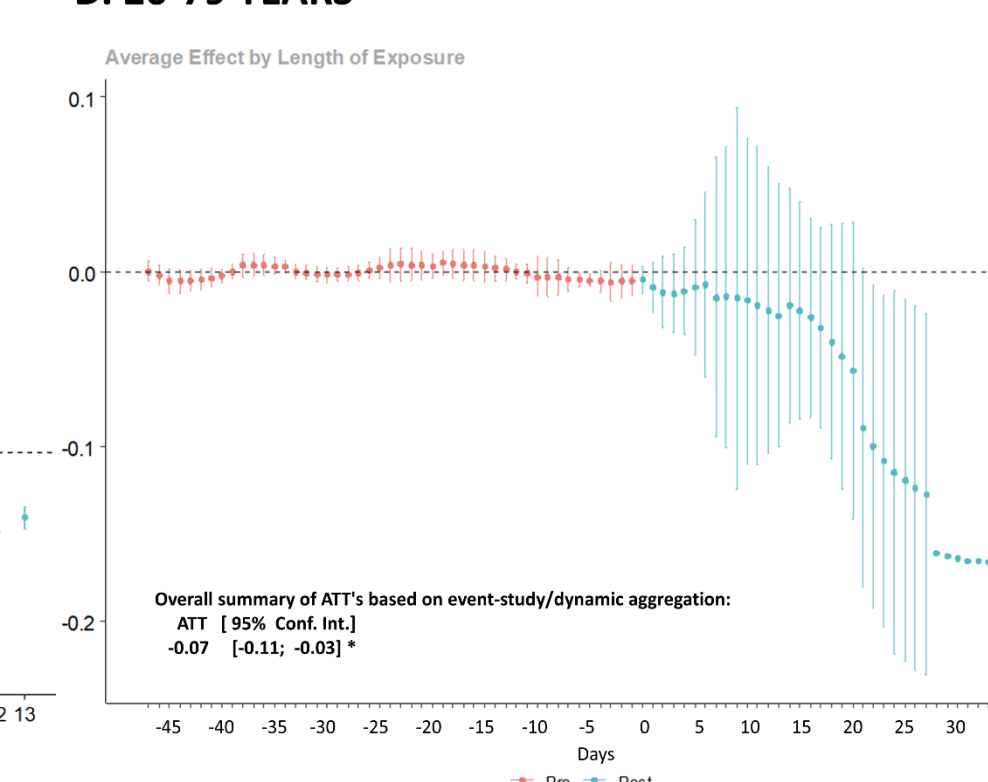
E. 0-19 YEARS OLD



B. 20-79 YEARS OLD



D. 20-79 YEARS



F. 20-79 YEARS OLD

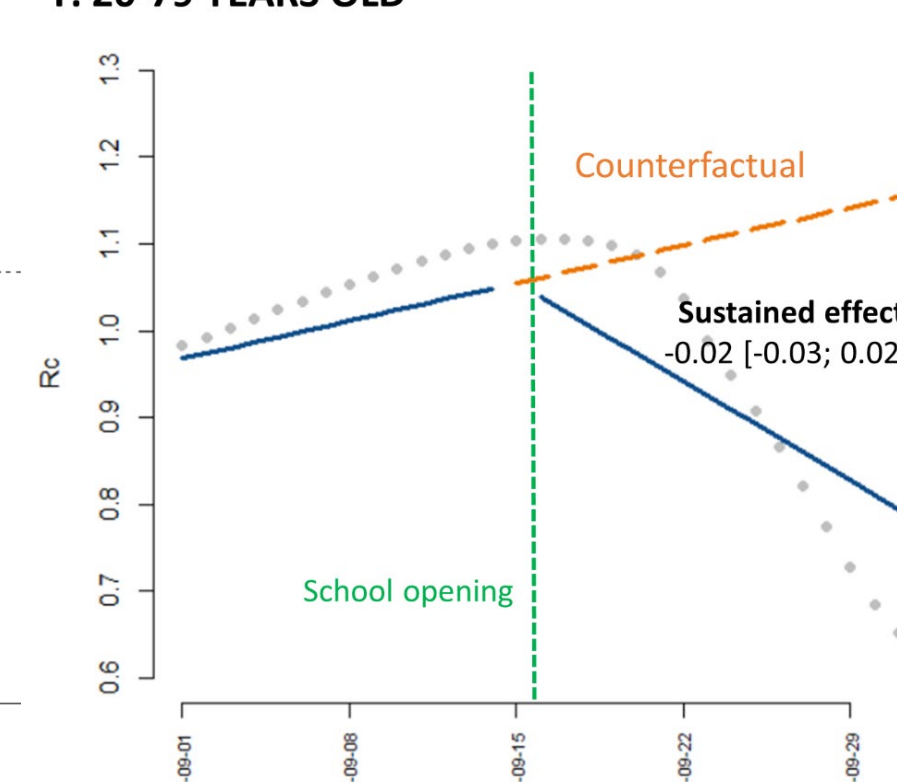


Figure 5. Staggered DID analysis: In red are the estimates of the average treatment effect for the treated subpopulation (ATT) at the points in time before school reopening; in blue are the estimates of ATT at the points in time equal or following school reopening in: A. the student population and B. the adult population of Italy, in C. the student population and D. the adult population of Germany. **ITS analysis:** The gray dots are the daily R_c values. In blue is the regression line estimated by the ITS model. The orange line is the **counterfactual** scenario, i.e. the line of the expected R_c values if the trend observed before the reopening of schools had persisted. * indicates a statistically significant estimate (p -value<0.05).

In Italy and Germany, post-reopening R_c estimates were significantly lower compared to those from regions/states that had not yet reopened at the same time-points, both in the student population (Overall Average Treatment effect for the Treated subpopulation (O-ATT): -0.80 [95%CI:-0.94;-0.66] for Italy; O-ATT:-0.30 [95%CI:-0.36;-0.23] for Germany) and the adult population (O-ATT:-0.04 [95%CI:-0.07;-0.01] for Italy; O-ATT:-0.07 [95%CI:-0.11;-0.03] for Germany). In Portugal, there was a significant decreasing trend in R_c following school reopenings compared to the pre-reopening period (sustained effect: -0.03 [95%CI:-0.04; -0.03] in students; -0.02 [95%CI:-0.03; -0.02] in adults).

Multivariable models adjusting for confounders confirmed these results.

CONCLUSIONS

Preliminary results indicate that the Lolli-Methode may be useful to decrease SARS-CoV-2 infections in the school setting, which are greater in teachers than in students. The trends of SARS-CoV-2 in autumn 2022 appeared to be driven mainly by the geographical location, seasonal changes and overall population behavior than by school openings.

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