

A dive into the wastewater-based epidemiology of SARS-CoV in Switzerland

Colloque scientifique mensuel ESD

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7 November 2023

Disease surveillance

Definition (*Langmuir, 1963*):

Surveillance, when applied to a disease, means the continued watchfulness over the distribution and trends of incidence through the systematic collection, consolidation and evaluation of morbidity and mortality reports and other relevant data.

Objectives of disease surveillance (*Declich, 1994*)

To describe the **ongoing patterns** of disease:

- ▶ identify trends and acute changes

To link with **public health action**:

- ▶ disease investigation and control
- ▶ health services planning
- ▶ evaluation of measures

To study the **natural history** and epidemiology of diseases:

- ▶ not limited to those diseases for which effective control measures are available

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Historical origins of disease surveillance



Figure 1: The quarantine hospital on Lazzaretto Vecchio island was at the center of Venice's vast [public health response](#) to the Black Death in the 14th century (*Wikimedia commons*).

Historical origins of disease surveillance

The Diseases and Casualties this Week.

A Bortive	6	Kingevil	10
Aged	54	Lethargy	1
Apoplexic	1	Murthered at Stepney	1
Bedridion	1	Palsie	2
Cancer	2	Plague	3880
Childbed	23	Plurisie	1
Chriomes	15	Quinsie	6
Collick	1	Rickets	23
Consumption	174	Rising of the Lights	19
Convulsion	88	Rupture	2
Dropie	40	Sciatica	1
Drowned 2, one at St. Kath. Tower, and one at Lambeth	2	Scowring	13
Feaver	353	Scurvy	1
Fistula	1	Sore legge	1
Flax and Small-pox	10	Spotted Feaver and Purples	190
Flux	2	Starved at Nurse	1
Found dead in the Street at St. Bartholomew the Less	1	Stillborn	8
Frighted	1	Stone	2
Gangrene	1	Stopping of the stomach	16
Gowt	1	Strangury	1
Grief	1	Suddenly	1
Griping in the Guts	74	Surfeit	87
Jaundies	3	Teeth	113
		Thrush	3
		Tifick	6

Figure 2: In 17th-century London, in response to recurrences of bubonic plague, authorities instituted the weekly publication of a Bill of Mortality detailing the number of burials with cause of death (Wellcome Library).

Historical origins of disease surveillance

-
- 1888: Mandatory reporting of eleven communicable diseases and death certificates, in Italy
 - 1893: Publication of international list of causes of death by the International Statistical Institute (founded in London in 1885)
 - 1911: Use of surveillance data from National Health Insurance, in the United Kingdom
 - 1935: First National Health Survey, in the USA
 - 1943: First registry, the Danish Cancer Registry
First Sickness Survey, in the United Kingdom
 - 1965: Establishment of an Epidemiological Surveillance Unit in the Division of Communicable Diseases at WHO headquarters, Geneva
 - 1966: First publication of Communicable Disease Surveillance Reports by WHO
 - 1967: Development of General Practitioners' Sentinel Systems, in the United Kingdom and the Netherlands
-

Figure 3: Developments of disease surveillance since the end of the 19th century (*Declich, 1994*).

Infectious disease surveillance today

Passive surveillance:

- ▶ mandatory notification of cases by doctors and labs
- ▶ administrative data (encoded hospital billing data)
- ▶ vital statistics

Active surveillance:

- ▶ outbreak investigation
- ▶ sentinel systems
- ▶ population-based surveys
- ▶ wastewater-based epidemiology

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Background

Wastewater-based epidemiology (WBE):

- ▶ first proposed by Daughton (2001) for monitoring **illicit drugs**
- ▶ extension to pharmaceuticals, tobacco, alcohol, pesticides, heavy metals... (Choi, 2018)
- ▶ extension to **infectious diseases** (Mao, 2020)

Background

WBE for infectious disease surveillance:

- ▶ early warning signals (identify circulating pathogens/variants)
- ▶ spatio-temporal trends?

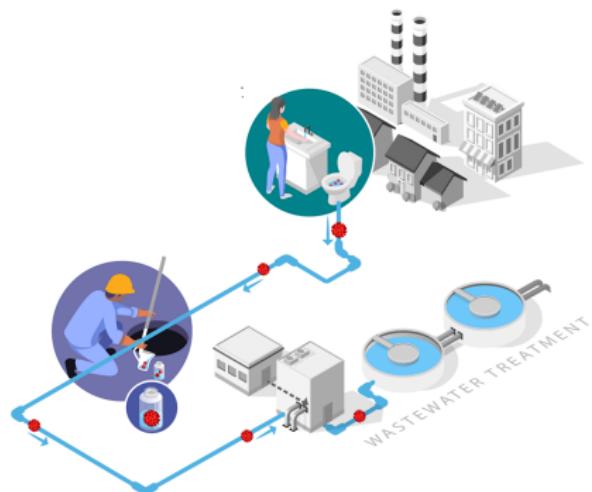


Figure 4: WBE for infectious disease surveillance (*CDC*).

Background

Data-generating mechanism:

- ▶ SARS-CoV-2 incidence
- ▶ Fecal shedding profile (1-2 weeks, up to 7 months)
- ▶ Circulation in wastewater pipes, sample collection
- ▶ Quantification with RT-PCR

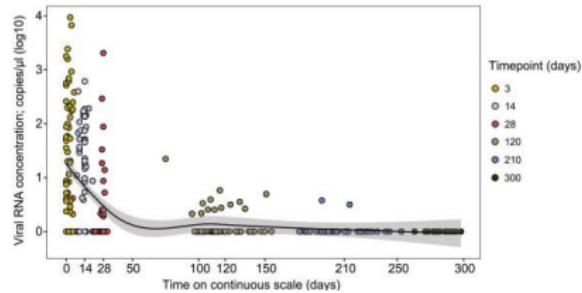


Figure 5: Fecal viral RNA concentration in stool samples over time (*Natarajan et al., 2022*).

Data

Wastewater surveillance of SARS-CoV-2 in Switzerland:

- ▶ started 7 February 2022
- ▶ maximal 118 wastewater plants (ARA for *Abwasserreinigungsanlagen*)
- ▶ fluctuations in the number of ARAs, down to 14 after July 2023
- ▶ various sampling frequencies (3 to 6 times per week)
- ▶ samples sent to 9 different laboratories (1 lab after July 2023)
- ▶ 22367 total measurements as of 18 September 2023

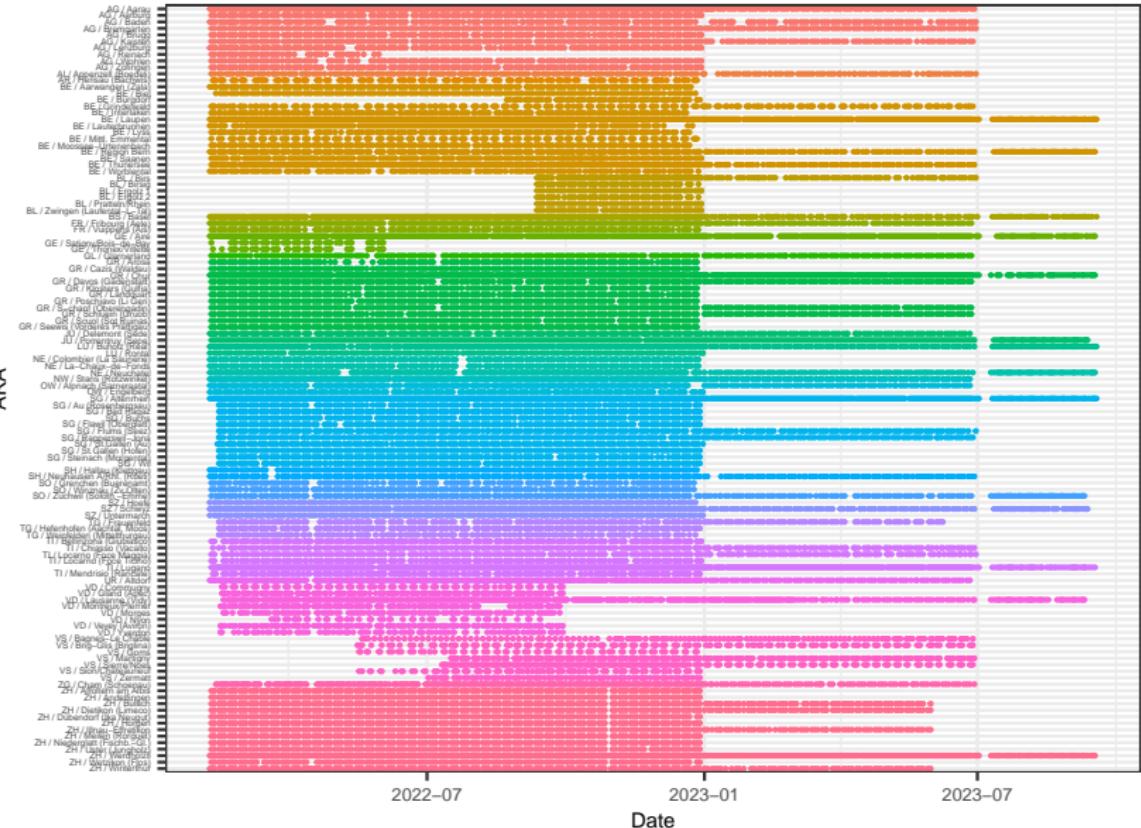
Data

Raw data consists of **concentrations** in gene copies per liter [gc/L]

- ▶ account for **wastewater flow** [m³/day] (rain, activity...)
- ▶ account for **population** covered by the ARA
- ▶ formula for **viral load per population** [gc/day/100,000 population]

$$VL = \frac{\text{concentration} \times \text{flow} \times 1,000}{\text{population}/100,000}$$

Data



Data

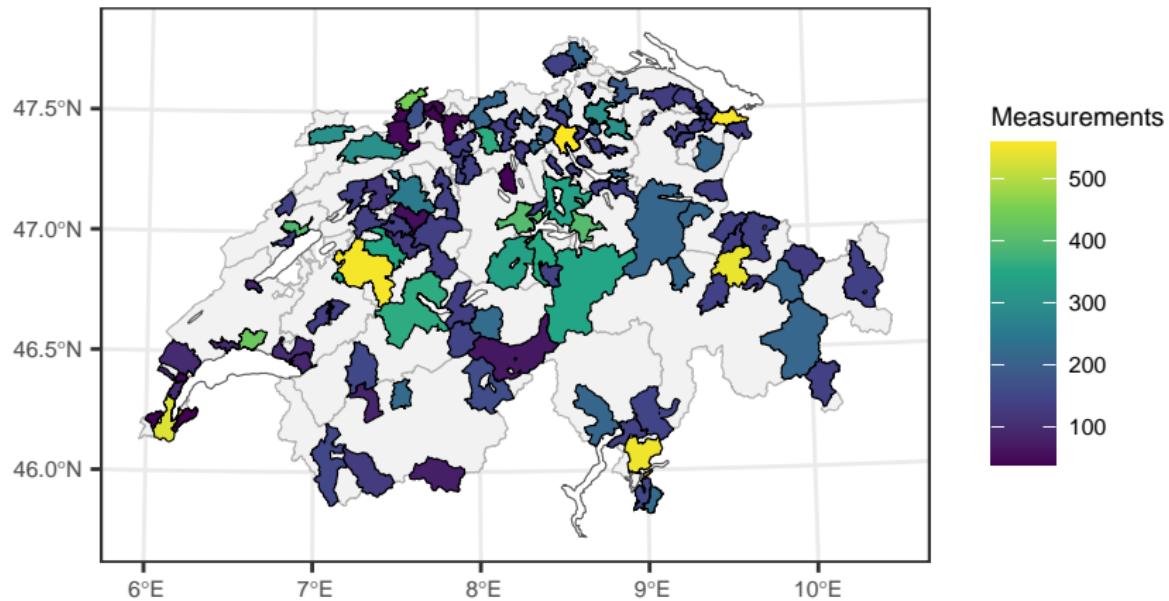


Figure 6: Number of viral load measurements by ARA.

Data

Large heterogeneity across time and space:

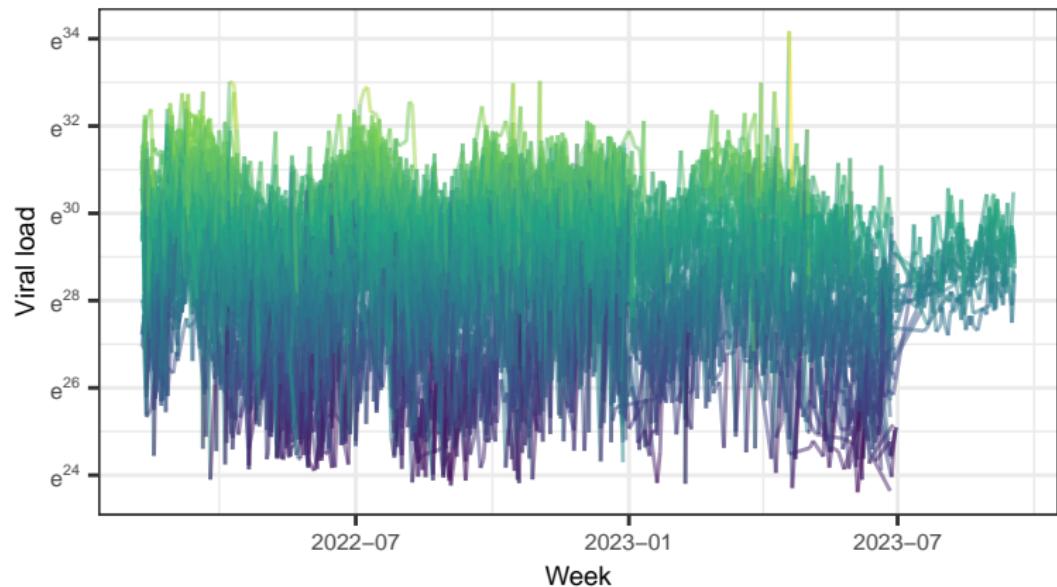


Figure 7: Daily SARS-CoV-2 viral load in wastewater by ARA (removing values below the LOD or LOQ).

Data

Difficulties of interpretation:



Figure 8: Viral load in wastewater as of 31 October 2023, Lausanne VD (Vidy) (*FOPH dashboard, covid19.admin.ch*).

Objectives

1. Disentangle the various sources of heterogeneity
 - ▶ laboratory, quantification method, systematic temporal or spatial effects, remaining noise...
2. Extract a clean, "noise-free" temporal signal
 - ▶ at the national and/or regional level
3. Assess the agreement with other types of surveillance
 - ▶ confirmed cases, hospitalizations, Sentinella, CH-SUR, pooled tests...

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Objectives

4. Forecasting/nowcasting
 - ▶ historical data, LFO validation
5. Future surveillance strategies
 - ▶ site selection, sampling frequency, rotation

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Methods

Space-time model based on gamma regression, accounting for:

- ▶ limits of detection (LOD) and of quantification (LOQ)
- ▶ systematic temporal effects (public holidays, weekends)
- ▶ national time trend (RW2)
- ▶ systematic shift for each ARA (IID)
- ▶ deviations from national trend for each ARA (RW1)
- ▶ effect of laboratory and quantification method

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Results

Posterior predictive check (model fit) is quite good.

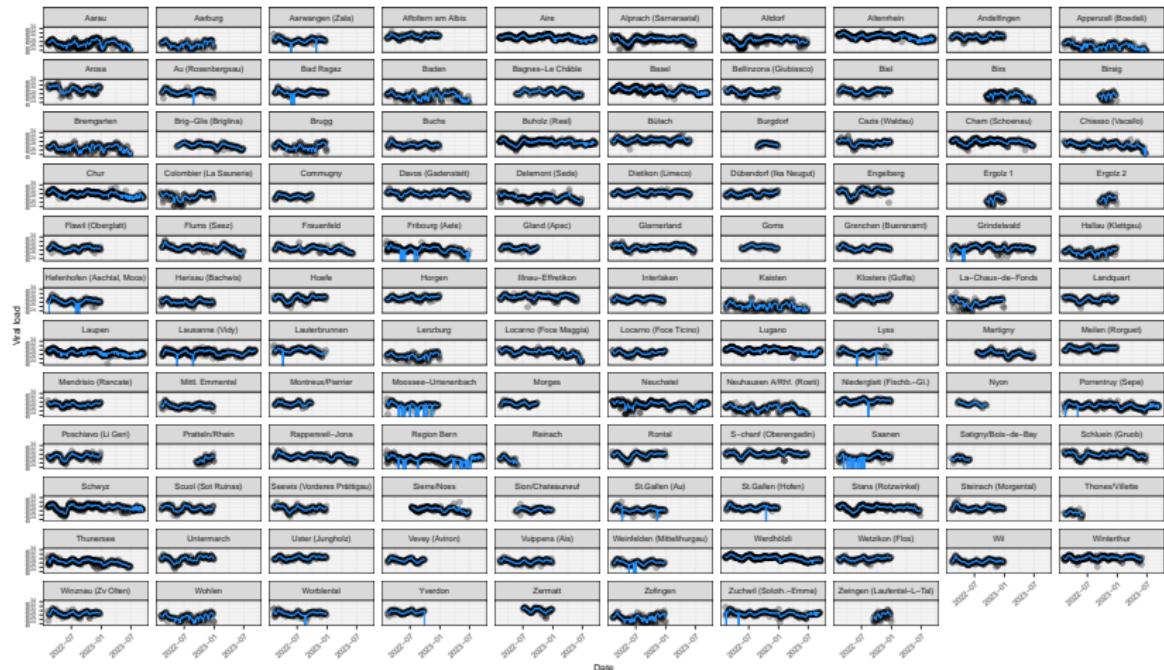


Figure 9: Model fit.

Results

Posterior predictive check ([model fit](#)) is generally quite good.

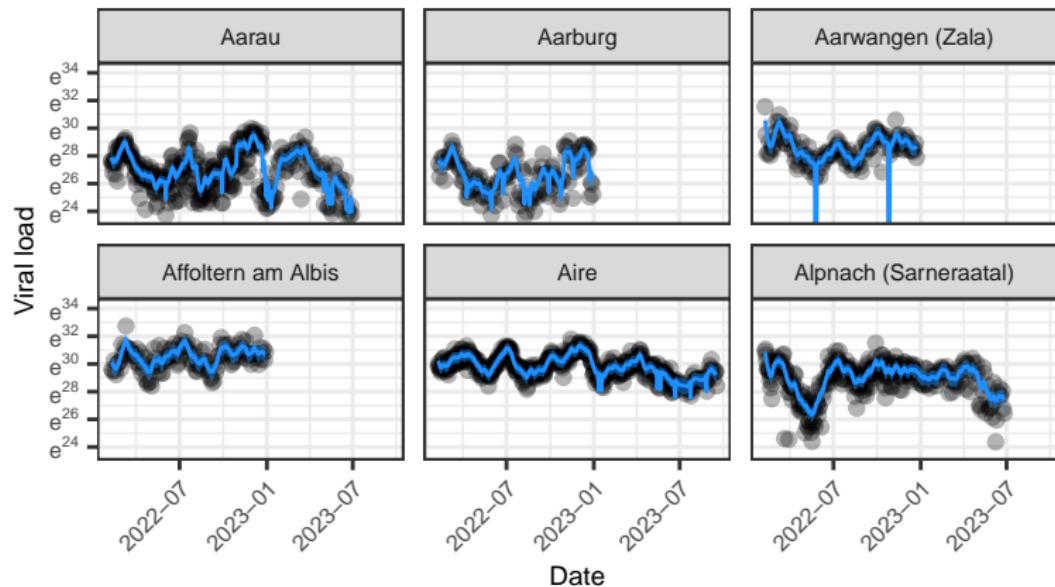


Figure 10: Model fit.

Results

Effect of laboratory and method (reference is EAWAG_0):

- ▶ $\exp(\beta)$ can be interpreted as a relative viral load, e.g., the viral load is *on average* 1.39 times higher (0.88 to 2.18) in KLZH than EAWAG_0

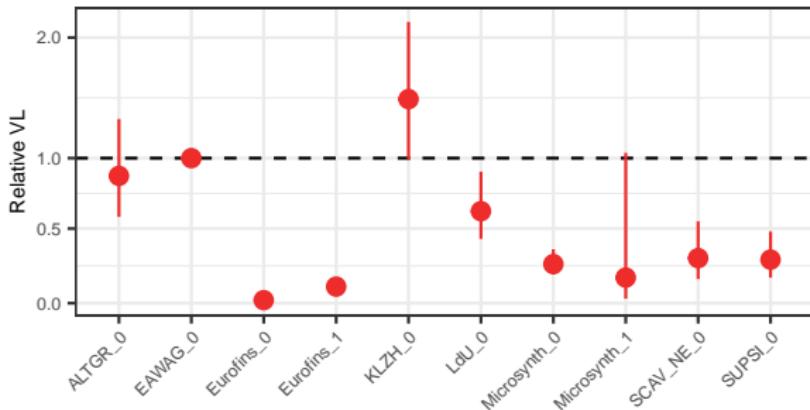


Figure 11: Estimated effect of laboratory (laboratory name) and method change (marked by 0 and 1).

Results

Effect of public holidays and weekends:

- ▶ no clear influence

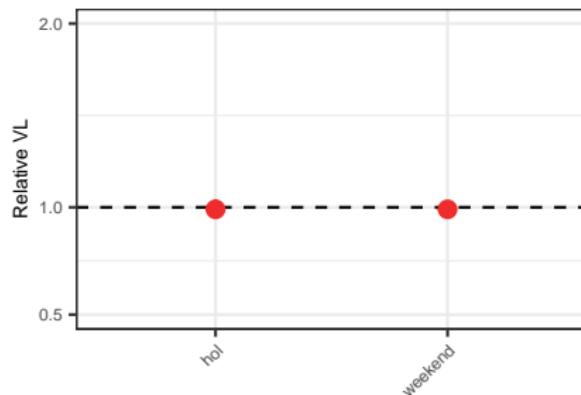


Figure 12: Estimated effect of holidays and weekends.

Results

Effect of specific ARAs:

- ▶ some ARAs have consistently higher or lower viral loads
- ▶ may be issues with **population** covered (tourism...)

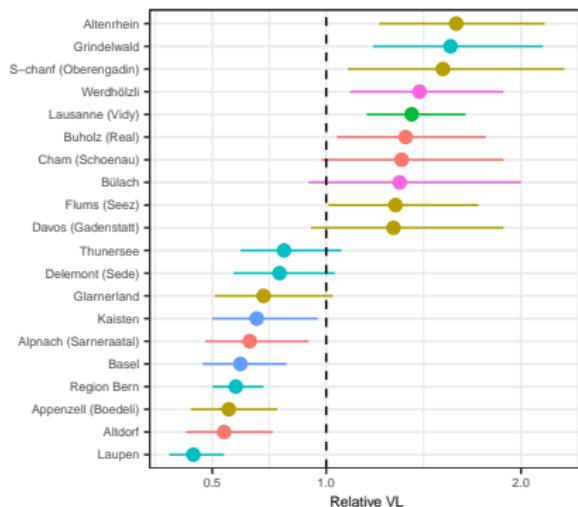


Figure 13: Estimated ARA-specific effects.

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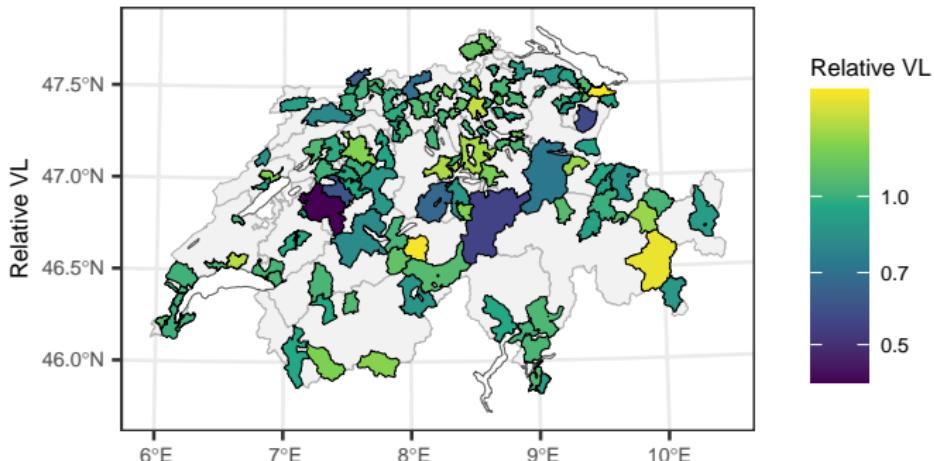


Figure 14: Estimated ARA-specific effects.

Results

Average temporal trend at the national level:

- ▶ accounts for all aspects described before

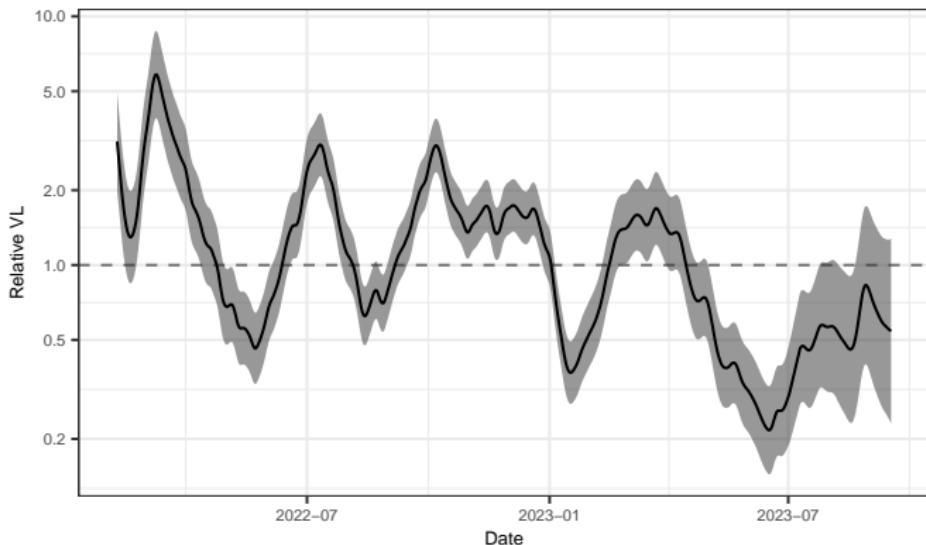


Figure 15: Estimated average temporal trend at the national level.

Results

Residual deviations from the average temporal trend:

- ▶ come on top of all aspects described before

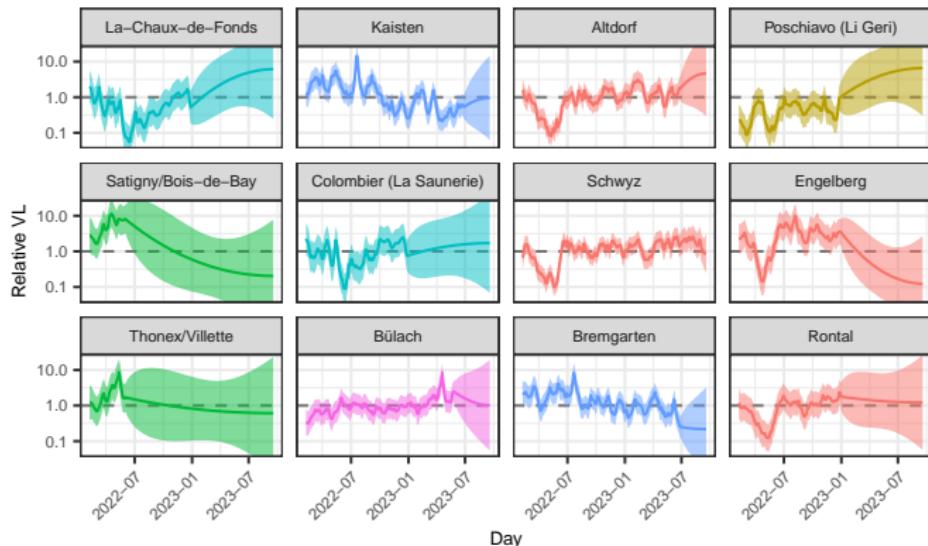


Figure 16: Residual deviations from the average temporal trend (top 12 on absolute value).

Discussion

1. Disentangle the various sources of heterogeneity
 - ▶ important heterogeneity across laboratories and ARAs
 - ▶ no clear effect of weekends and public holidays
 - ▶ possible issue with population covered (tourism and/or mistake)
2. Extract a clean, “noise-free” temporal signal
 - ▶ national time trend
 - ▶ local trends to identify special situations (Neuchâtel-Jura / Berner Oberland)

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Future work:

- ▶ Additional covariates: socio-economic position (SEP), population density, urban/rural, working population, ethnicity...
- ▶ Assess the agreement with other types of surveillance (obj. 3; joint modelling of reported cases/hospitalizations and viral load)
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Acknowledgements

FOPH: Anna Fesser, Moritz Wagner, Katrin Schneider

ETHZ: James Munday, Tanja Stadler

EAWAG: Tim Julian, Christopher Ort