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

Colloque scientifique mensuel ESD

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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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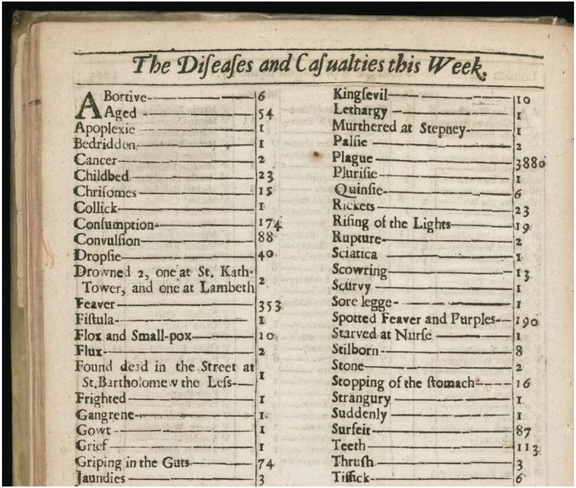
Historical origins of disease surveillance

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.

Abortive	6	Kingſevil	10
Aged	54	Lethargy	1
Apoplexie	1	Murthered at Stepney	1
Bedridden	1	Palſie	2
Cancer	2	Plague	3880
Childbed	23	Pluriſie	1
Chriſomes	15	Quinſie	6
Collick	1	Rickets	23
Conſumption	174	Riſing of the Lights	19
Convulſion	88	Rupture	2
Dropſie	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
Flox 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	Stilborn	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
		Tiffick	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

Infectious disease surveillance today

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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?

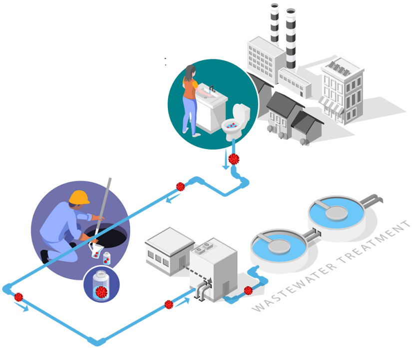


Figure 4: WBE for infectious disease surveillance *(CDC)*.

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

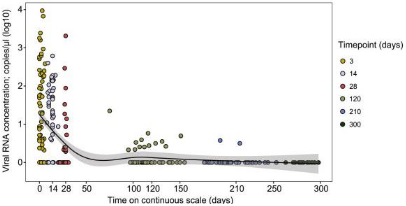


Figure 5: Fecal viral RNA concentration in stool samples over time *(Natarajan et al., 2022)*.

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

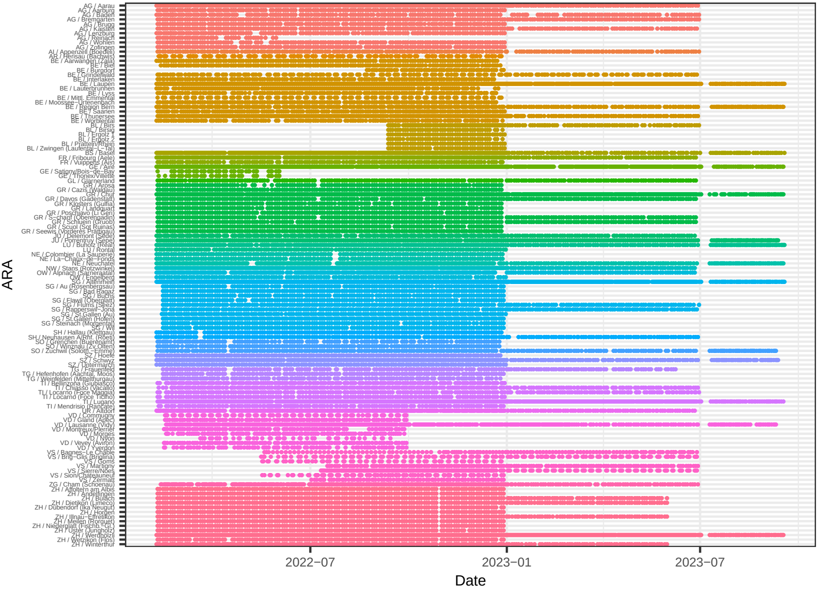
Data

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



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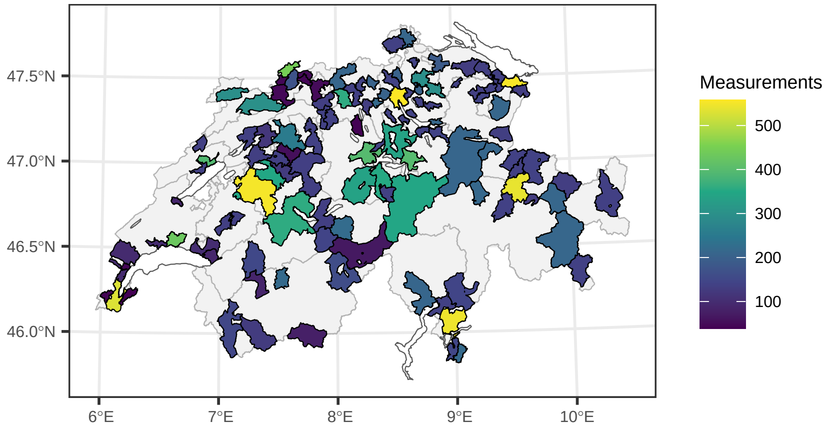

Figure 6: Number of viral load measurements by ARA.

Data

Large heterogeneity across time and space:

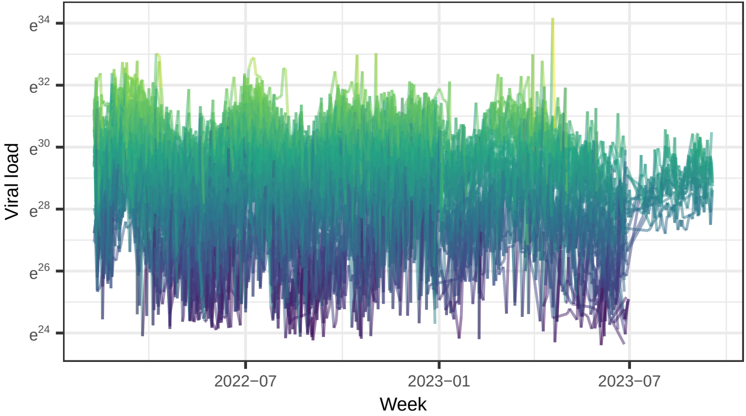

Figure 7: Daily SARS-CoV-2 viral load in wastewater by ARA (removing values below the LOD or LOQ).

Difficulties of interpretation:

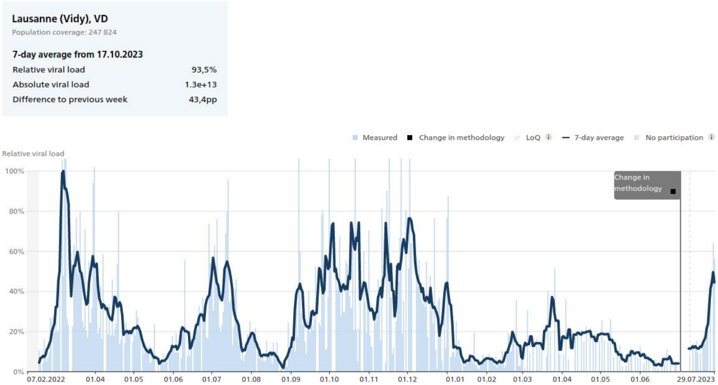

Figure 8: Viral load in wastewater as of 31 October 2023, Lausanne VD (Vidy) *(FOPH dashboard, covid19.admin.ch)*.

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.

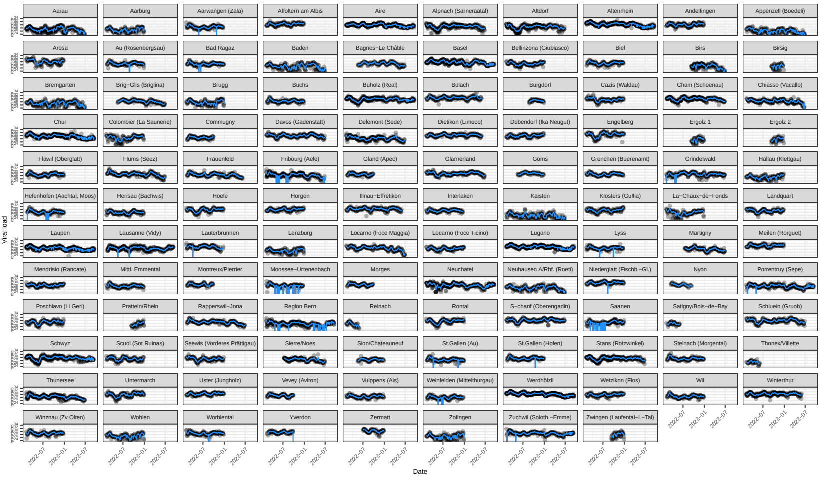

Figure 9: Model fit.

Results

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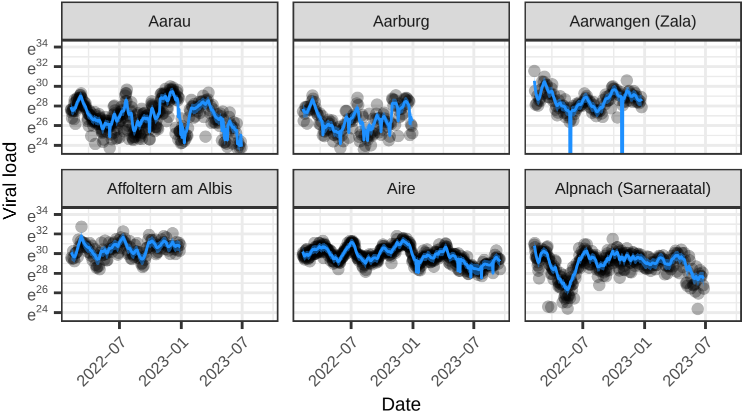

Figure 10: Model fit.

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

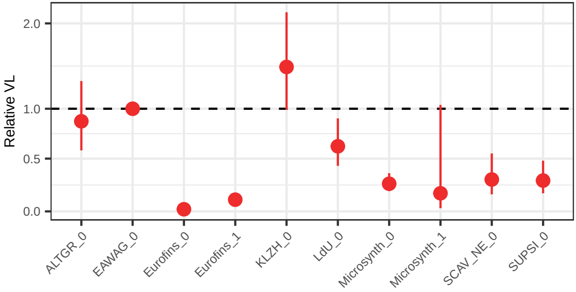

Figure 11: Estimated effect of laboratory (laboratory name) and method change (marked by 0 and 1).

Results

Effect of public holidays and weekends:

- no clear influence

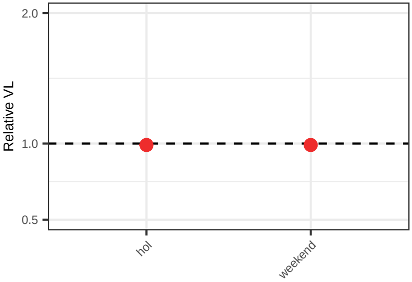

Figure 12: Estimated effect of holidays and weekends.

Results

Effect of specific ARAs:

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

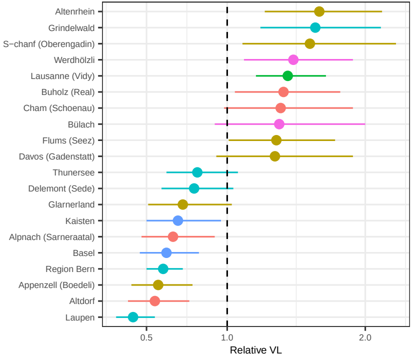

Figure 13: Estimated ARA-specific effects.

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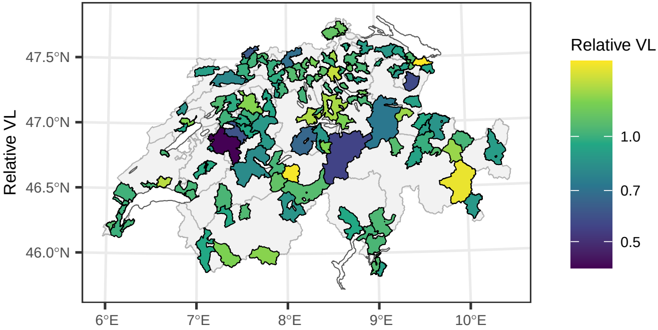

Figure 14: Estimated ARA-specific effects.

Results

Average temporal trend at the national level:

- accounts for all aspects described before

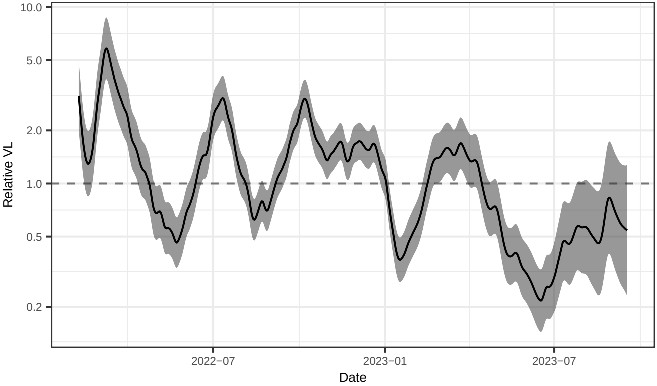

Figure 15: Estimated average temporal trend at the national level.

Results

Residual deviations from the average temporal trend:

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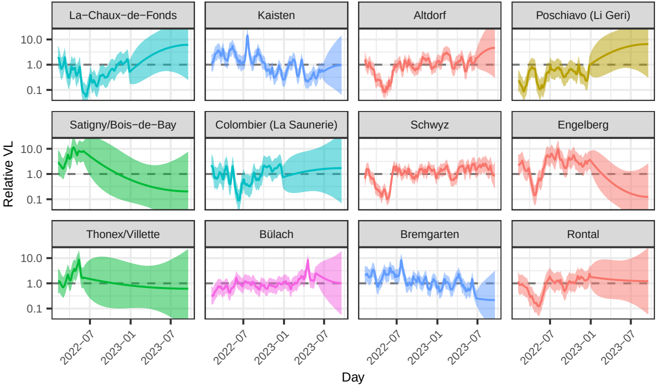

Figure 16: Residual deviations from the average temporal trend (top 12 on absolute value).

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. . .
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