Evaluation of the Pilot Wastewater Surveillance for SARS-CoV-2 in Norway

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Introduction

Environmental surveillance by means of detecting pathogens in wastewater has a long history in public health, particularly for monitoring poliovirus, reaching back to the 1940's[1]. More recently, during the 90's this approach has received increased interest as a population-based tool to detect pharmaceuticals, drugs and antimicrobial resistance - AMR[2]. In the context of the ongoing COVID-19 pandemic, wastewater-based epidemiology (WBE) has evolved rapidly being explored and implemented by several countries as a supplemental tool to detect and monitor signals of SARS-CoV-2 transmission in communities, including variants information [3]. During the pandemic, the public health institute (NIPH) has been closely following the research developments and trends within this field by monitoring peer review publications and international guidance documents as well as participation in international networks for wastewater surveillance (EU JRC, WHO protocol for Water and Health)[4]. As of April 2021, the European Commission recommended member states to establish a systematic surveillance of SARS-CoV-2 and its variants in wastewater [5]. This led to intensified discussions about the relevance and benefits of setting up a parallel WBE-system in Norway to complement clinical surveillance data which was becoming even more relevant when the TISK-strategy[6] was downscaled during the fall-winter season 2021-2022 as population immunity increased. Consequently, testing captured by the national surveillance systems was largely replaced by rapid antigen self-tests. Thus, the traditional, individual-based test data used to monitor disease trend in the population became less reliable. Still, there was a risk for new waves and new virus variants with immune-evading abilities urging the need for strengthening the existing surveillance systems by introducing alternative data sources to cover the lowest level of the surveillance pyramid (Figure 1). Following these premises, FHI decided to set up and finance a pilot project to develop, test and implement wastewater-based surveillance of SARS-CoV-2 and its variants. The aim of the pilot was to i) complement and support existing national surveillance systems for SARS-CoV-2 in terms of a) early warning of new waves and trend monitoring and b) detection and monitoring

[1] Trask JD, Paul JR. Periodic examination of sewage for the virus of poliomyelitis. The Journal of Experimental Medicine. 1942 Jan 1;75(1):1.

[2] Chau KK, Barker L, Budgell EP, Vihta KD, Sims N, Kasprzyk-Hordern B, Harriss E, Crook DW, Read DS, Walker AS, Stoesser N. Systematic review of wastewater surveillance of antimicrobial resistance in human populations. Environment international. 2022 Apr 1;162:107171.

[3] https://wastewater-observatory.jrc.ec.europa.eu/; https://www.arcgis.com/apps/dashboards/c778145ea5bb4daeb58d31afee389082

[4] Hyllestad S, Myrmel M, Lomba JA, Jordhøy F, Schipper SK, Amato E. Effectiveness of environmental surveillance of SARS-CoV-2 as an early warning system during the first year of the COVID-19 pandemic: a systematic review. Journal of Water and Health. 2022 Aug;20(8):1223-42.

[5] EC C(2021) 1925. Commission recommendation on a common approach to establish a systematic surveillance of SARS-CoV-2 and its variants in wastewater in the EU

[6] Testing, isolation quarantine and contact tracing strategy in combination with abortion of all non-medical interventions

of new variants of concern and ii) to explore the usefulness of wastewater-based surveillance for future preparedness.

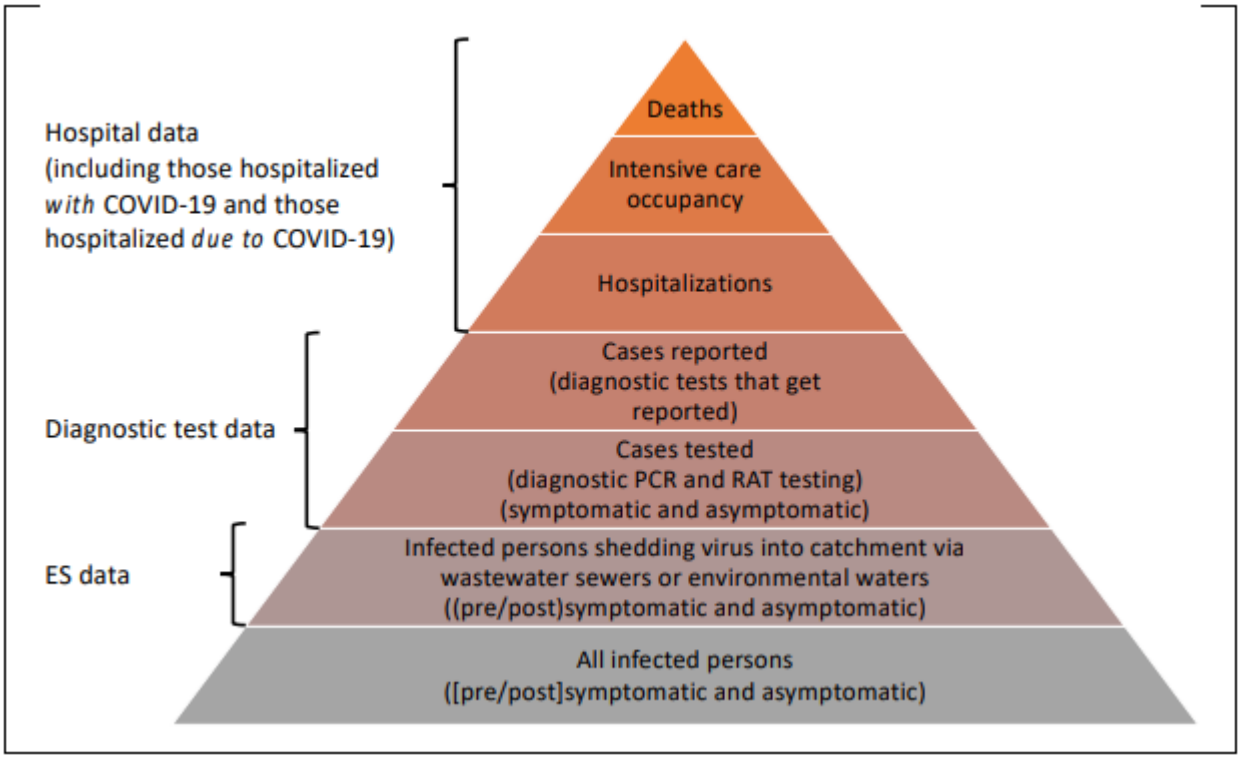

Figure 1 Disease pyramid (from WHO interim guidance https://www.who.int/publications/i/item/WHO-HEP-ECH-WSH-2022.1)

Aim and objectives of the surveillance system evaluation

The aim of this evaluation is to describe and evaluate the Norwegian pilot wastewater surveillance for SARS-CoV-2 in order to assess i) the performance relative to the aims of the system, ii) the benefits (e.g. added value) of implementing the system compared to, or as an alternative to, existing surveillance systems, and iii) opportunities and barriers in using WBE in future preparedness against public health threats. For the surveillance performance the following attributes will be evaluated:

- Sensitivity, specificity, and timeliness
- Usefulness
- Representativeness
- Simplicity
- Flexibility
- Acceptability
- Stability and reliability

When possible, attributes will be compared with other surveillance indicators that have been implemented in response to the COVID-19 pandemic in Norway.

Methods

Study design and data sources

The evaluation will be carried out as a descriptive analysis and consist of the following three components: (i) description of the WWS system, (ii) identification of end-users and stakeholders and (iii) analysis of the system's attributes and performance (sensitivity, specificity, timeliness, usefulness, representativeness, simplicity, flexibility, stability, and communication).

A combination of the following data sources will be used:

i) Survey to obtain information from the stakeholders and end-users.
ii) Technical assessment of data collected and reported through the pilot of the wastewater surveillance system.
iii) Technical assessment of the information reported in NIPH's weekly surveillance reports on COVID-19, influenza and other respiratory diseases.
iv) Direct information from members of the pilot project team.
v) Open-source literature (scientific *peer review* and grey).

The evaluation will consist of the following four steps:

Step 1. Description of the pilot wastewater surveillance system

The first step consists of describing the system, taking into account the different elements of the systems. The following elements will be described: surveillance objectives, type of surveillance, population under surveillance, methods for data collection and analysis, data structure, reporting format, surveillance system outputs.

Step 2. Identification of stakeholders of the surveillance system

A stakeholder is defined as either a) end-user" of the system, e.g. public health officials who receives data and information from the system as part of their roles and responsibilities during the COVID-19 pandemic, b) any actor responsible for providing data and information to the system.

Step 3. Analysis of the surveillance system performance attributes

The third step will focus on the evaluation of the performance of the system using international guidelines on evaluation of public health surveillance systems as reference.

Considering that the attributes as defined in the guidelines for evaluation of surveillance systems given by the European Centre for Disease Prevention and Control (ECDC)[7] and the U.S. Centers for Disease Prevention and Control (CDC)[8] are tailored for clinical surveillance systems, we will adapt the definitions of these attributes (Table 1) to fit a wastewater-based surveillance system and the specific purpose of the pilot WWS system in Norway.

Whenever possible the performance of the wastewater surveillance system will be compared with the performance of other national COVID-19 surveillance systems that were active during the pilot (study) period.

[7] ECDC. Data quality monitoring and surveillance system evaluation. A handbook of methods and applications. 24 Sep 2014. Accessible at www.ecdc.europa.eu/en.
[8] German RR, Lee LM, Horan JM, Milstein RL, Pertowski CA, Waller MN. Updated guidelines for evaluating public health surveillance systems: recommendations from the Guidelines Working Group. MMWR Recomm Rep. 2001;50(Rr-13):1-35; quiz CE1-7.

Table 1. Wastewater surveillance attributes and their definitions as used in this study, adapted from ECDC and CDC guidelines

Attribute	Definition
Sensitivity	The proportion of waves of infection or new virus variants that are captured by the WWS system.
Specificity	The system's ability to avoid false warnings about new waves of infection or new virus variants (false positives)
Timeliness	The ability of the WWS to deliver timely results and to provide an early warning signal compared to other surveillance systems.
Usefulness	The extent to which the system has benefited the end-users and led to specific public health actions, either in the form of assessments or measures.
Representativeness	The proportion of the population covered by the WWS. The concordance between the geographical area covered by the WWS and the geographical unit for clinical surveillance considered for other indicators is evaluated.
Simplicity	The structure/organization of the system and its ease of operation, including logistics from sampling to reporting of results.
Flexibility	The ability of the system to adapt to changes over time being able to be scaled up, scaled down or expand if necessary.
Acceptability	The extent to which end-users and stakeholders were willing to participate in the pilot WWS and in the future.
Stability	The ability to collect samples and produce results without deviation or failure.
Communication	The ability of the system to deliver information and data in a clear and distinct manner.

Sensitivity, specificity and timeliness

Our evaluation will be based on descriptive comparison of results obtained from the WWS with other relevant clinical indicators available during the pilot period (June 2022 – March 2023), and feedback from end-users, stakeholders and NIPH's experts. Cross-correlation analysis will be performed to assess the wastewater systems' ability to provide early warning signal of new waves of infection. The analysis will be performed using time series data. The time series will include data from epidemiological waves of infection detected during the study period (from week 33, 2022 to week 10, 2023).

The performance of the wastewater surveillance system in terms of detection and monitoring of new variants of concern (e.g., mutational PCR screening, sequencing data) will be compared with the results of the clinical virological surveillance program.

Usefulness - public health impact

Usefulness implies that surveillance results are used for public health action. Assessing usefulness includes taking inventory of actions or decisions that have been taken in conjunction with the surveillance system. A public health surveillance system is useful if it contributes to the prevention and control of adverse health-

related events, including an improved understanding of the public health implications of such events. The usefulness of the pilot wastewater surveillance system will be assessed in a broader sense including both direct actions and decisions as well as other uses as reported by the end-users. Usefulness of the pilot will be assessed through questionnaire to the stakeholders. Furthermore, we will search scientific literature and open web sources for examples of usefulness of similar systems in other European countries.

Representativeness

A public health surveillance system that is representative accurately describes the occurrence of a health-related event over time and its distribution in the population. Knowledge on the representativeness of surveillance data on the national level is important for some of the proposed specific objectives of EU-wide surveillance. Examples of situations that could affect representativeness are uneven geographical coverage, prevalence of urban vs. rural reporting sites, and minority populations not reached by the surveillance systems. Representativeness of the pilot wastewater system will be assessed by descriptive analysis of the system (e.g., coverage) and its catchment areas. Furthermore, we will perform simple calculations to test the impact on the overall results of excluding data from one or more sampling sites.

Simplicity

A surveillance system should be as simple as possible while still meeting the surveillance objectives. Simplicity refers to the structure/organization of the system and its ease of operation, including logistics. Simplicity of the pilot wastewater system will be assessed through descriptive analysis of the system.

Flexibility

A flexible public health surveillance system can adapt to changing information needs or operating conditions with little additional time, personnel, or allocated funds. Flexible systems can accommodate, for example, new health related events/threats/pathogens, changes in case definitions or technology, and variations in funding or reporting sources. In addition, systems that use standard data formats (e.g., in electronic data interchange) can be easily integrated with other systems and thus might be considered flexible. The flexibility of the pilot wastewater system will be assessed by descriptive analysis of the system, considering the possibility of using the system in monitoring other agents of relevance.

Acceptability

Acceptability reflects the willingness of persons and organizations to participate in the surveillance system and contribute with data. Acceptability of the pilot wastewater surveillance system will be assessed through questionnaire to the stakeholders.

Stability

Stability refers to the reliability (i.e., the ability to collect, manage, and provide data properly without failure) and availability (the ability to be operational when needed) of the public health surveillance system. Stability and reliability of the pilot wastewater system will be assessed through descriptive analysis of the system.

Communication

Communication refers to the frequency, format of reporting, and use of different media for distribution of results and information about the pilot wastewater-based surveillance system. This will be assessed by collecting data from the FHI communication department (e.g., number of citations in media over time) as well as through questionnaire to the stakeholders.

Step 4. Propose recommendations

The 4th step offers recommendations on how to address the results of the evaluation.

Quality assurance

This protocol was developed by Ettore Amato and Elisabeth Madslien. Internal FHI experts and experts from other European countries (RKI/DE and HAS/UK) were consulted in the planning phase and will be consulted during the project, when needed.

To reduce the risk of bias, two independent advisors at FHI, outside of the pilot project team, reviewed the protocol and results before publication.

Limitations

Performance and added value of the system might vary in different stages of the pandemics, dependent on which variants that are present and the control measures (in particular test strategy) that are in place. Furthermore, seasonal variations might occur due to effects of temperature and precipitations.

The study was performed at a late stage of the pandemic when population immunity was high and testing activity was low. This means that using test data would not be a reliable reference indicator when comparing performance attributes. Since estimates about the "true" prevalence in the population was lacking we decided to use hospital data as reference, knowing that this would only capture "the tip of the iceberg" and with considerable lag in terms of time.

Protection of human subjects

No sensitive information or personal health information will be collected through the evaluation study. All data collected from the stakeholders will be analyzed in an aggregated manner without referring to names or the specific affiliations they represent. However, due to the limited number of stakeholders, we cannot exclude that data from the questionnaires could indirectly be linked to the person that contributed with information, based on the role and affiliation of the person.

Thus, informed consent will be collected from the stakeholders before data collection stating they should answer on the behalf of the organization they represent.

Furthermore, results from the questionnaire should only be shared and published upon approval from the contributing stakeholders.

Data ownership

FHI is the owner of all data collected in this study.

Outputs and publications

A report will be produced from this project. The evaluation report with findings and recommendations will be communicated to the main stakeholders. The language of the report will be Norwegian.

Additionally, an abstract for ESCAIDE conference will be drafted from some of the findings.

Part of the results from the pilot, including sequencing results and detailed quantitative analysis of performance and predictive value, might be suitable for publications in scientific *peer review* journals.

All publications from this work will be in line with the *Vancouver* guidelines on authorship.

Sourcing of funding and conflict of interest

This project will be funded through institutional resources. The principal investigators declare that they have no conflict of interest.

Appendix

A. Questionnaires for end-users and stakeholders

A.1 - Questionnaire for wastewater treatment plants

Background information
1. Which unit/department do you represent? (Fill in) 2. What is your role/responsibilities? (Fill in)
About future wastewater surveillance and collaboration
3. How has the collaboration with the laboratory and those who collect the samples worked? Is there anything that could have been done better? (Describe briefly) 4. How has the collaboration with NIPH worked? Is there something that you have missed or that could have been done better? (Describe briefly) 5. What capacity do you have to continue with sampling for this type of surveillance in the future, beyond the test period? (Describe briefly) 6. What will be the biggest challenges for you related to continuing with sampling for this type of purpose? (Describe briefly)

A.2 – Questionnaire for public health authorities at local level

Background information
1. Which municipality do you represent? (Fill in) 2. Which unit/department do you represent? (Fill in) 3. What is your role? (Fill in) 4. What main tasks and areas of responsibility has your unit/department had in connection with the pandemic? (Fill in)
Previous knowledge of wastewater surveillance (prior to NIPH pilot)
5. Do you know whether your municipality has been involved in previous projects where wastewater has been used to map information about the health status of the inhabitants of your municipality? **Yes ☐ No ☐ Unsure ☐** 6. If yes, what type of mapping? (tick) a. Antimicrobial Resistance (AMR) ☐ b. Other infectious diseases ☐ c. Chemical substances/medicines/narcotics ☐ d. Other (please specify) …
Communication
7. Which of the following information channels do you use to keep yourself updated on the results of the wastewater surveillance? (tick) a. Result report sent by e-mail from NIPH ☐ b. NIPH's weekly report (weekly report for COVID-19, influenza, and other respiratory infections ☐

c. The project's website (https://www.fhi.no/hn/statistikk/overvaking-smittsomme-sykdommer-i-avlopsvann/) ☐
d. Other professional actors/channels ☐

8. If you have to choose, through which of the channels mentioned above do you prefer to receive results from the wastewater surveillance? **a.** ☐ **b.** ☐ **c.** ☐ **d.** ☐
9. Which parts of the results did you find most interesting and relevant to the task you are responsible for? (Describe briefly)
10. Do you think the results were understandable and sufficient for the tasks you are responsible for? **Yes**☐ **No**☐ - If no, what do you think could have been done better/differently? (Describe briefly)
11. Is there anything you are missing in the results reports you have received from NIPH? (Describe briefly)
12. Are you satisfied with how frequently you have received results report from NIPH? **Yes, satisfied**☐ **No, could be more frequent** ☐ **No, could be less frequent** ☐
13. Are there any other actors/units in your municipality that you think would benefit from being involved in the project and/or receiving results reports? **Yes** ☐ **No**☐ **-** If "yes", which actors/units? (Describe briefly)

Usefulness

14. In what way have the results been used in your municipality? (Describe briefly)
15. Have the results from the wastewater surveillance been useful to you?

Yes ☐ **No**☐ **Unsure** ☐ **-** If yes, in which way? (Describe briefly)

16. Do you know of any specific measures or assessments that have followed from the results of the wastewater surveillance? **Yes** ☐ **No**☐**.**
    a. If "yes", briefly describe which measures/assessments?
    b. If "no", what do you think is the most important obstacle to the results being able to be used for specific measures or assessments? (Describe briefly)
17. What type of information would be useful to know about the wastewater surveillance besides the information you have received? (Describe briefly)
18. Based on experiences from the test project, do you think that you would have benefited from the results of the project if the wastewater surveillance would have been started earlier in the pandemic, i.e., before June 2022? **Yes** ☐ **No** ☐
    a. If "yes", during which phase of the pandemic do you think you would have benefited the most from wastewater surveillance? **2020** ☐ **2021** ☐ **2022 (prior to June** ☐ Please explain why (describe briefly):

Implementation and cooperation

19. How did you experience the collaboration with NIPH in connection with the project, do you have any suggestions for something that could have been better? (Describe briefly)

About future wastewater surveillance

20. Would you be willing to continue participating in the wastewater surveillance if extended beyond the test period, i.e., after March 2023? **Yes ☐ No ☐ Unsure ☐** 21. Are there any challenges to participating from your side and, if so, what are the biggest obstacles? (Describe briefly) 22. Which other diseases/health threats do you think will be most relevant to include in wastewater-based surveillance in the future, and which will have the highest relevance for you? (Please explain why)
Suggestion for improvement
23. Do you/you have other suggestions on how we can improve the system?

A.3 – Questionnaire for risk assessors and managers at national level

A.3.1 Questions for the Directorate of Health

Background information
1. Which unit/department do you represent? 2. What is your role/responsibilities?
Usefulness and future use
3. Have you benefited from the results of NIPH's pilot for wastewater surveillance of SARS-CoV-2? In what way? What do you think the results can be used for in the future? (Describe briefly) 4. How do you consider the usefulness of the wastewater surveillance compared to other indicators used in the national monitoring of SARS-CoV-2? (Describe briefly) 5. From a public health perspective, do you have any thoughts about future areas of use for wastewater surveillance? (Describe briefly) 6. What do you think will be the most important prerequisites for wastewater surveillance to be used as a national preparedness tool in dealing with future epidemics and health threats? (Describe briefly)

A.3.2 Questions for the Norwegian Institute of Public Health

Background Information
1. Which unit/department do you represent? 2. What is your role/responsibilities?
Usefulness, limitations, and future applications
3. Have the results of the SARS-CoV-2 wastewater surveillance pilot been useful? In what way? (Describe briefly) 4. Seen from a national surveillance perspective, will there be a need for wastewater surveillance beyond March 2023? **Yes ☐ No ☐ Unsure ☐** 4.1. If yes, at what level and what do you think the results can be used for in the future? (Describe briefly) 5. Have the results been communicated in an understandable way? Do you have suggestions for improvements in the way we present the results? (Describe briefly) 6. What do you think are the most important limitations of the results from the wastewater surveillance? (Describe briefly) 7. How do you assess the usefulness of the wastewater surveillance compared to other indicators used in the national surveillance of SARS-CoV-2? (Describe briefly)

8. Are there other parts of the surveillance that can be scaled down in the future if we continue with wastewater surveillance? (Describe briefly)
9. If the project had started earlier during the pandemic, do you think the results would have had an impact on NIPH's risk assessments and advice regarding measures? (Describe briefly)
10. From a public health perspective, do you have any thoughts about future areas of use for wastewater surveillance? If the surveillance is to be extended to other agents, which ones do you think should have the highest priority and why? (Describe briefly)
11. What do you think will be the most important prerequisites for wastewater surveillance to be used as a national preparedness tool in addressing future epidemics and health threats? (Describe briefly)