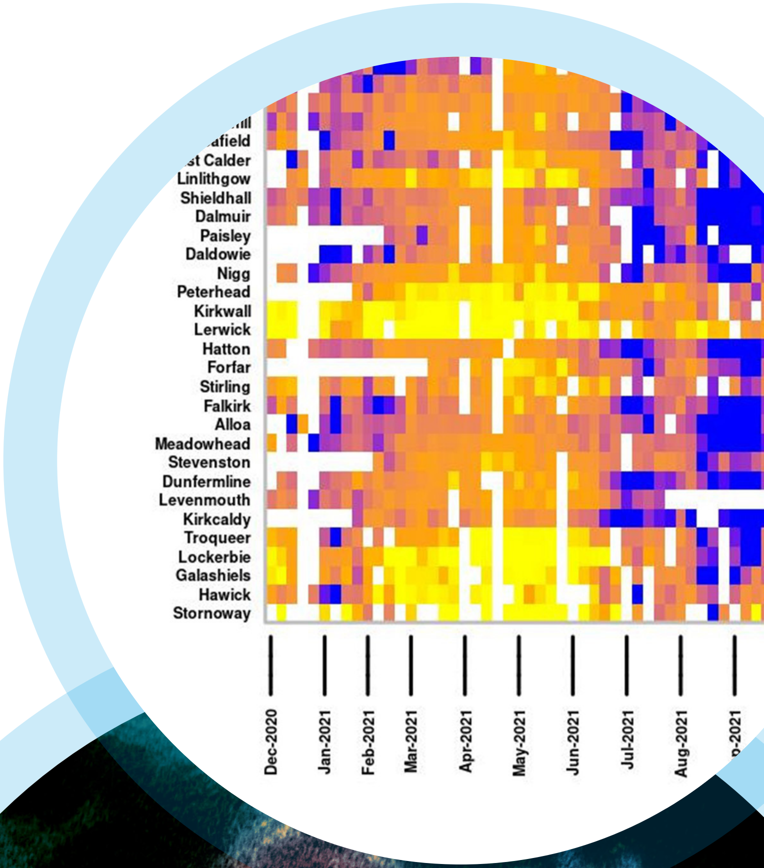
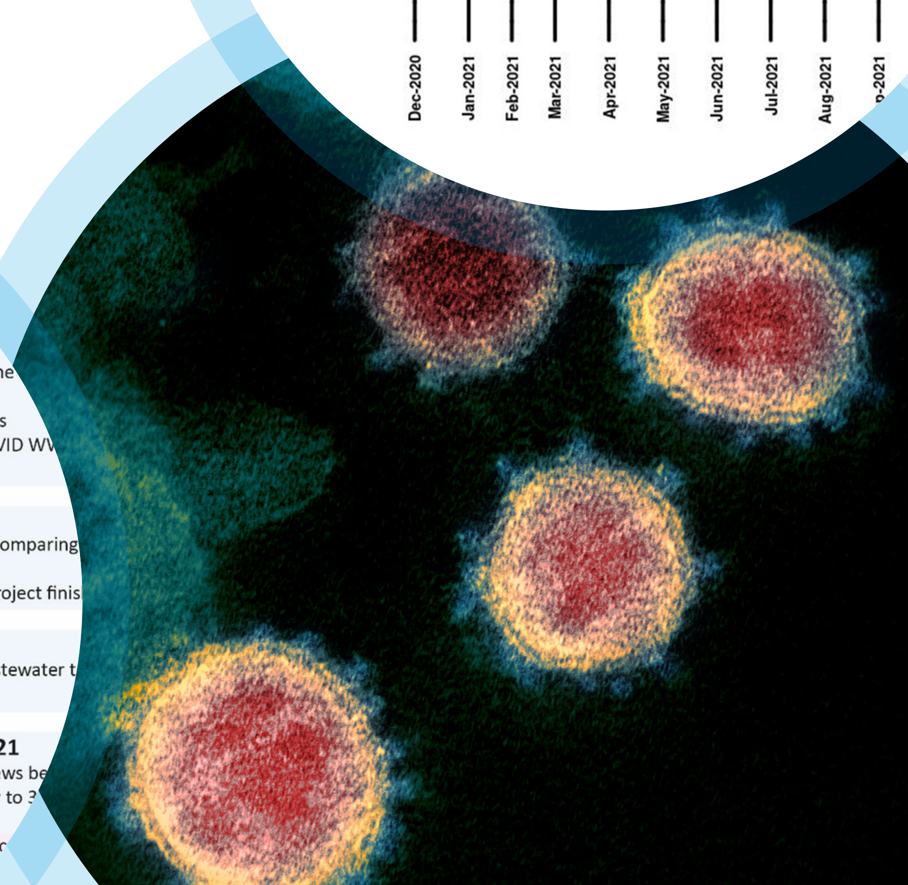
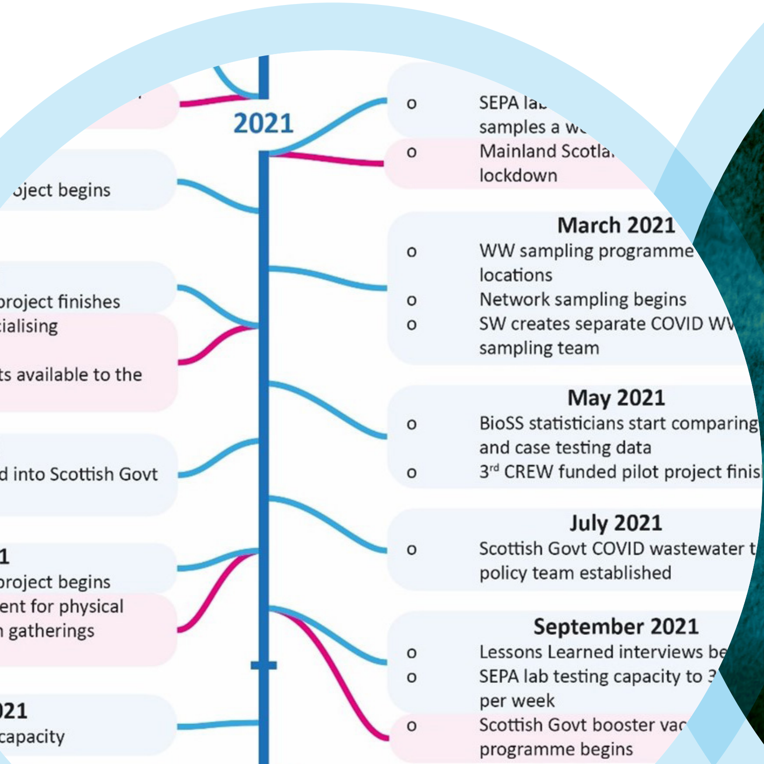
CENTRE OF EXPERTISE FOR WATERS

SARS-CoV-2 monitoring in Scottish wastewater: Variant Detection, FAIR data Outputs, and Lessons Learned

Appendices







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CENTRE OF EXPERTISE FOR WATERS

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Contents

Preface

This CREW Combined Technical Appendices document informed the basis of the Main Report on 'SARS-CoV-2 monitoring in Scottish wastewater: Variant Detection, FAIR data Outputs, and Lessons Learned' (ISBN: 978-1-911706-07-6), commissioned by Scotland's Centre of Expertise for Waters (CREW).

This combined document consists of four appendices:

- **Appendix 1** – Open Research data paper preprint citation and link.
- **Appendix 2** – Consent form for learning review of SARS-CoV-2 wastewater testing.
- **Appendix 3** – Learning review SARS-CoV-2 wastewater testing programme.
- **Appendix 4** – Good practice in qualitative research methods in the social sciences.

Executive Summary

Background

The virus that causes Covid-19 disease, SARS-CoV-2, is excreted by infected people into the sewage system. Genetic material from the virus can be detected in wastewater samples that are collected before treatment in wastewater plants. Scottish Government and its agencies monitored SARS-CoV-2, in wastewater from June 2020 to the date of this report. This CREW research project built upon the programme of monitoring for SARS-CoV-2 in Scottish wastewater, which had been active for over a year when this project started.

Research objectives

1. **A method to detect variants of the SARS-CoV-2 virus in wastewater (see section 2).**

   The laboratory test used in Scotland since 2020 tested the total amount of SARS-CoV-2 viral material in wastewater samples, without distinguishing between the variants of the virus. This research objective aimed to test which variant(s) were present in the wastewater samples, which required different laboratory techniques. Trials of three alternative methods were commissioned from molecular genetics researchers at the Institute of Genetics and Cancer, led by Prof. Nick Gilbert.

   The research project was not tasked with nationwide monitoring. In response to the wave of the Omicron variant in December 2021, however, the researchers agreed to and delivered variant detection in wastewater across Scotland for six months.

2. **Sharing outputs from the wastewater monitoring programme by Open Research methods (see section 3).**

   The SARS-CoV-2 wastewater monitoring programme focused on delivering results for immediate use, reporting to Scottish Government and to the public. This research objective aimed to identify, prepare and share other technical products from the programme for different audiences, particularly researchers and other practitioners. The Biological Research Data Management team (Bio_RDM) led by Dr Tomasz Zielinski was commissioned to share the programme's outputs using the best Open Research practices of the scientific community.

3. **Lessons Learned from the development and management of the programme (see section 4).**

   Monitoring SARS-CoV-2 in wastewater was a new capability, developed and delivered by people and organisations working in a new partnership, under time and budget pressure. The success of the programme depended upon the ways that they worked together, as well as on the technical sampling, testing and reporting methods. This research objective aimed to identify and document the working methods, structures and interactions that contributed to this partnership in Scotland, analysing aspects of the programme that had been successful and where improvements might be made in future. The technical capabilities of the programme were not the focus here. Social scientists Dr Isabel Fletcher and Prof Catherine Lyall from Science, Technology and Innovation Studies (STIS) were commissioned by CREW to gather and analyse this information, to compare the experience in Scotland with other countries, and to infer any general lessons and recommendations for Scottish Government and its agencies in delivering future, urgent programmes.

Research undertaken

1. The 'Variant Detection' research project tested three lab methods, quantitative Reverse-Transcriptase Polymerase Chain Reaction (qRT-PCR or qPCR), digital droplet PCR (ddPCR or dPCR) and 'next generation' DNA sequencing. A sequencing-based method was implemented for nationwide monitoring, in an extension to the research that also involved data scientists from Biomathematics and Statistics Scotland (BioSS).
2. The Open Research team trained the laboratory researchers in Open Research methods; prepared laboratory notebooks and the protocols for laboratory and analytical methods; compiled a reference set of the monitoring data up to February 2022, along with visual displays of those data; and shared these new outputs from the programme.
3. The Lessons Learned research interviewed 41 participants in the programme (see section 4.2 in report, study design); reviewed documents from the Scottish and international wastewater monitoring programs; and analysed the interview transcripts and documentary evidence (see appendices 2-4).

Results

1. DNA sequencing was the best method to detect SARS-CoV-2 variants in wastewater. The research team delivered variant detection from wastewater across Scotland for six months, capturing the spread of the Omicron variant from December 2021 and the BA.2 variant in the Spring of 2022, and refined detection methods in the process.
2. The Open Research team shared the programme's technical outputs in six different ways, online and in person, with a web Homepage linking to all the resources. Open Research methods for particular outputs and particular audiences promise to deliver further value from the investment in this and similar programmes. This project found that there is still a knowledge gap regarding FAIR data management practices, among both academic and non-academic partners. Training and further adoption of such practices could streamline the delivery of future projects and increase their long-term impact.
3. The Lessons Learned research found that the Scottish SARS-CoV-2 wastewater testing programme was an impressive achievement: a nationwide surveillance programme for a novel organism was developed collaboratively from a "standing start" in less than six months. This success was due to a combination of high-level support from key individuals within relevant organisations and the hard work and motivation of those working on the project. However, after this impressive start the programme encountered some organisational issues that made the transition from innovative research to a routine testing programme challenging (even taking account of the accelerated timescales involved).

Recommendations

1. DNA sequencing data will likely be valuable inputs to Scottish policy post-Covid-19, for example in monitoring other pathogens or Anti-Microbial Resistance genes, both in wastewater and in other environmental samples. Significant technical expertise is required to establish and adapt the laboratory and bioinformatic analysis methods, which are both areas of rapid innovation. This might best be delivered by a partnership of delivery agencies and molecular genetics researchers.
2. Future partnerships should establish a shared data resource early on, with support for good data management from the start, to assist both programme delivery and dissemination of outputs.

The key recommendations from the Lessons Learned review are:

3. Stronger cross-government and inter-agency links among those working in the environment and health sectors are needed to tackle future crises. Some of these recommendations address how to support those links.
4. A well-founded and responsive national research capacity requires an appropriate balance of public support for project and core funding to ensure the availability of key research infrastructure and capacity.
5. The Scottish Government could make better use of its network of Chief Scientific Advisors as a conduit for information exchange among the research and policy communities.
6. The Scottish Government should establish a new post of Chief Scientist for Public Health to better represent the Scottish Public Health community in light of the increasing need to focus on "One Health" strategies. The review findings indicate that neither the Chief Scientist (Health) nor the Chief Medical Officer currently represent or provide sufficiently high-profile leadership for the Scottish Public Health community.
7. The Scottish Government should consider adopting the good practice of the RESAS-funded knowledge brokerage units such as CREW and establish similar bodies for the Scottish Public Health community that bring researchers and stakeholders together to co-create research on policy-related topics.
8. Ensure ongoing support to enable groups (such as CAMERAS) to meet and maintain professional networks. These are a cost-effective way of future-proofing crisis responses and funding for such activities should be protected.

Appendix 1: Open Research paper (2022)

"SARS-CoV-2 RNA levels in Scotland's wastewater", Livia C. T. Scorza, Graeme J. Cameron, Roisin Murray-Williams, David Findlay, Julie Bolland, Brindusa Cerghizan, Kirsty Campbell, David Thomson, Alexander Corbishley, David Gally, Stephen Fitzgerald, Alison Low, Sean McAteer, Adrian M. I. Roberts, Zhou Fang, Claus-Dieter Mayer, Anastasia Frantsuzova, Sumy V. Baby, Tomasz Zieliński, Andrew J. Millar. *Scientific Data.* DOI : 10.1038/s41597-022-01788-3.

Appendix 2: Consent Form for Learning Review of COVID Wastewater Testing

Please tick the appropriate boxes	Yes	No
Taking Part		
I confirm that I have read and understood the Participant Information document for this study and I have been given the opportunity to ask questions.	☐	☐
I understand that I am free to refuse to answer any question during the interview.	☐	☐
I agree to the interview being recorded and later transcribed	☐	☐
I understand that my taking part is voluntary; I can withdraw from the study at any time and I do not have to give any reasons for why I no longer want to take part.	☐	☐
Use of the information I provide for this project only		
I understand my personal details such as name, phone number and address will not be revealed to people outside the project.	☐	☐
I am content for my words may be quoted anonymously in publications, reports, web pages, and other research outputs.	☐	☐
I am content for my affiliation or role (e.g., research scientist, government official etc.) to be used in reports publications when I am being quoted.	☐	☐
I understand that while the research team will take care to maintain anonymity, they cannot guarantee that people will not be able to identify you, given the small number of people in research communities.	☐	☐
Use of the information I provide beyond this project		
I agree for the data I provide to be archived anonymously at the UK Data Archive.	☐	☐
I understand that other authenticated researchers will have access to this data only if they agree to preserve the confidentiality of the information as requested in this form.	☐	☐
I understand that other authenticated researchers may use my words in publications, reports, web pages, and other research outputs, only if they agree to preserve the confidentiality of the information as requested in this form.	☐	☐

__________________________________ ______________________ ________

Name of participant [printed] Signature Date

__________________________________ ___________________ ________

Researcher [printed] Signature Date

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Appendix 3: Learning Review SARS-CoV-2 Wastewater Testing Programme – participant information sheet

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Project Aim

This project will review the development of the Scottish programme for SARS-CoV-2 wastewater testing to learn key lessons that can be used to inform future urgent responses to health and environmental crises. As social scientists experienced in analysing research collaborations across different disciplines and sectors, we will be interviewing members of the project team and their collaborators who successfully developed the initial wastewater testing programme.

We are interested in the following kinds of questions

- Which individuals and organisations have taken part in this research?
- When did they participate, what did they contribute and how did they do this?
- What was their experience of collaborating in this research – what helped them take part and what made it harder?
- What role did Scottish Government funding play in the successful development of this testing programme?
- What lessons can we learn to improve future responses to health and other emergencies?

Interviews will be conducted with research scientists from the University of Edinburgh and their key collaborators across the environment and health sectors.

This research is part of a larger project *Methodology for the Detection of new variants of SARS-CoV-2 in Wastewater* led by Professor Nick Gilbert of the University of Edinburgh Institute of Genetics and Cancer, and managed by CREW (the Centre of Expertise for Waters). The social science element of this research is led by Dr Isabel Fletcher of the University of Edinburgh School of Social and Political Science. It is funded by the Scottish Government.

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Appendix 4: Good practice in qualitative research methods in the social sciences

The Lessons Learned review adopted a qualitative research method which is often characterised by its inductive relationship between data and theory: empirical data are used to derive theory (or in this case, lessons learned), in contrast to the hypothesis-testing approach more commonly favoured by quantitative research methods (Thorne, 2000). The inherent value of a qualitative method lies in its ability to uncover new information, explore ambivalence, and investigate the reasons for views, in contrast to a quantitative approach to "measuring" opinion (Lyall and King, 2016). In this way, qualitative research can provide a "deeper" understanding of social phenomena than would be obtained from purely quantitative data (Silverman, 2000 p.8). However, the view persists in some quarters that governments favour quantitative research because it yields quick answers based on "reliable" variables (Silverman, 2000 p.2). This qualitative versus quantitative debate is most usually viewed by the social research community as specious: one approach is not "better" or "worse", but each yields different types of knowledge and good practice is to select the research paradigm best suited to the requirements of the research question (Patton, 1999).

This well-established social research methodology typically uses the voices of the research informants (in this case "interviewees"): direct quotes from interviews may be selected to provide detailed examples of more broadly made comments within the dataset as a whole. This approach is used to illustrate or emphasise a particular point being made in the narrative which is, itself, grounded in the summation of views on that topic. Given the non-probabilistic nature of the sampling in qualitative research (see below), it is not considered good practice to quantify respondents' views.

The empirical stage of qualitative research begins by defining the "case" under study. As noted in the text, this was a non-trivial task given the dispersed and ad hoc nature of the SARS-CoV-2 wastewater testing project given the pandemic conditions under which it was taking place. Identifying and enrolling participants required a variety of methods. These included desk research based on publicly available information, document analysis, initial scoping interviews and "snowballing" to yield a form of non-probability sampling typical of qualitative research (Bryman, 2012, pp.200-202). This enabled the construction of the stakeholder map (see Figure 9, main report) which identified for the first time, the key players in this SARS-CoV-2 wastewater testing programme. For a qualitative research study of this scale, 41 interviewees would be considered a substantial number. In most cases, interviewing stops once "data saturation" has been reached (Charmaz, 2014 pp. 213-216). We set out to interview as many representatives of the organisations identified in the stakeholder map as it was possible to identify, who were willing to be interviewed, within the timescale of the study.

This study was granted ethical approval by the School of Social and Political Science, University of Edinburgh. Consent procedures for interviews followed good practice in offering participants data confidentiality by excluding from the report any information that might enable participants to be identified (such as their areas of work or job title) as explained in Section 4.2 (main report) – see appendix 2.

Data analysis followed a grounded theory approach (Strauss and Corbin, 1994) with data collection and analysis taking place iteratively such that earlier findings contributed to questions asked during subsequent interviews. "Grounded theory" is a well-established method of data analysis, versions of which have been widely used by qualitative social scientists since its establishment in the 1960s. It provides guidelines for constructing an original theoretical analysis, enabling researchers to develop new ideas about their data and the conceptual issues raised by those data, unlike other approaches that use preconceived theories to shape the direction of the data analysis. Grounded theory uses a process called "coding" whereby researchers label, sort and organise the data. The first step in qualitative data analysis is thus one of data reduction and pattern identification (Caudle, 2004). In order to do this, transcripts from the interviews were coded using NVivo software[1]. "Coding" may be a misleading term for those unfamiliar with qualitative research methodologies: coding in qualitative data is an iterative, comparative process (unlike, for example, the quantitative analysis of survey data).

Our approach to data analysis in this study (in common with many other grounded theory approaches) reflects both the positivist and pragmatist epistemological underpinnings of grounded theory (Charmaz, 2014) where a series of key themes was also identified at the outset of the project through the research remit and early scoping interviews. So, in practice, coding takes place in two stages – "thematic coding" and "open coding".

The initial coding ("thematic coding") may be based on the themes identified in the literature review, which allows the researchers to interrogate the text, exploring and comparing data across the interviews. This enabled us to identify issues relevant to the analytical questions and to develop both a structure and an analytical narrative. This explains why a narrative

1 See https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home

literature review of the type reported in Section 4.3 is critical to the data analysis process (Bryman, 2012 p.9). The literature review provides a series of themes and topics that past researchers have previously identified which then form the basis of an analytical framework. These key themes from the literature act as “sensitising concepts” from which the thematic codes are derived.

This process of coding qualitative data is further elaborated in Box 1 and an illustration of “open coding” is given below.

Box 1: Description of coding process for qualitative data

…coding is a process whereby the data are broken down into their component parts and those parts are then given labels. The analyst then searches for recurrences of these sequences of coded text within and across cases and also for links between different codes. Thus, there is a lot going on in this process: the data are being managed, in that the transcripts are being made more accessible than if the researcher just kept listening and relistening to the recordings; the researcher is making sense of the data through coding the transcripts; and the data are being interpreted — that is, the researcher is seeking to link the process of making sense of the data with the research questions that provided the starting point, as well as with the literature relating to [the topic under study] and also with the theoretical ideas the authors use to illuminate the issue.

Bryman 2012 p.13

The second stage of data analysis (open coding) allows for a degree of flexibility beyond the confines of a fixed set of evaluation questions and permits the exploration of broader themes raised spontaneously by research participants. Thus, when “open coding” a dataset, qualitative analysts do not approach the data with a predefined set of questions (as one would in hypothesis testing). Instead, when we “open code” we are asking ourselves questions such as:

- Of what general category is this item of data an example?
- What is happening here?
- What does this item of data represent?

This allows us to construct new “categories” or “themes” not previously identified from our examination of the extant literature which in turn leads to theoretical reflections. So, to use an example cited by Bryman (ibid.):

A researcher might identify a series of words or phrases used by interviewees such as:

- At the *beginning*…
- She *used* to…
- It got much worse *later* on…

Taken together, these words and phrases indicate that there is a temporality to the phenomenon being discussed by different interviewees. But, significantly, none of the interviewees has specifically used the word “time”.

To give an example from our own study, when we analyse our interview transcripts, we hear interviewees describing a situation where “it was helpful to have someone who was able to interact at a higher level of authority” (Interview 22) and, elsewhere, we identify responses describing a lack of policy integration, poor communication between policy domains and lack of ownership of a policy arena which lead us to identify themes related to the need for high level advice and leadership.

Using this approach, we build up a rich picture of the situation and, informed by what we already know from previous academic research, we then combine empirical evidence from the data analysis with expert judgement to draw up a series of “lessons learned”. This method enables social researchers to develop a rigorous and integrated approach to data analysis. However, the nature of this method means that it is neither possible nor appropriate to quantify, hence we cannot specify “x number of interviewees say y”.

As reflexive social scientists, we then undertook a process of reflection and discussion among the research team and with other colleagues in the wider project team and steering group in order to review our methods and the results they had produced. This process included presentations at several project meetings at which stakeholders were present and a presentation and discussion session in the form of a webinar to which stakeholders were invited[2] which we have described as a way of “road testing” our findings in the text. During this event, participants were invited to contribute to an online poll to help us ratify and rank the order of priority that we should give our findings.

2 This online event was held on 27.5.22 and attended by participants from, inter alia, Public Health Scotland, SEPA, Scottish Government and Scottish Water.

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