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Computational analysis of SARS-CoV-2/COVID-19 surveillance by wastewater-based epidemiology locally and globally: Feasibility, economy, opportunities and challenges

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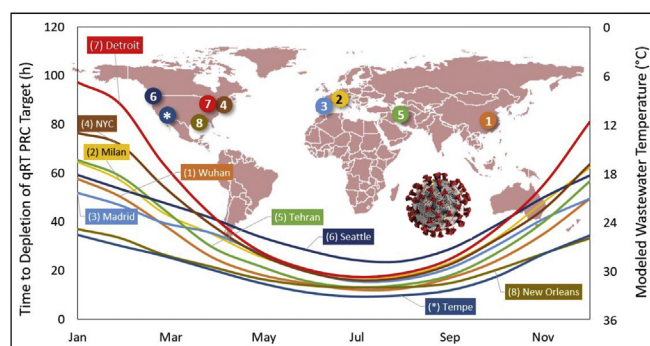
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HIGHLIGHTS

- Wastewater was computationally examined as a matrix for detection of SARS-CoV-2.
- One infected individual theoretically is detectable among 100 to 2,000,000 persons.
- Temperature and in-sewer travel time severely impact virus detectability.
- 2.1 billion people could be monitored globally in 105,600 sewage treatment plants.
- Combined use of WBE followed by clinical testing could save billions of US dollars.

GRAPHICAL ABSTRACT



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ABSTRACT

With the economic and practical limits of medical screening for SARS-CoV-2/COVID-19 coming sharply into focus worldwide, scientists are turning now to wastewater-based epidemiology (WBE) as a potential tool for assessing and managing the pandemic. We employed computational analysis and modeling to examine the feasibility, economy, opportunities and challenges of enumerating active coronavirus infections locally and globally using WBE. Depending on local conditions, detection in community wastewater of one symptomatic/asymptomatic infected case per 100 to 2,000,000 non-infected people is theoretically feasible, with some practical successes now being reported from around the world. Computer simulations for past, present and emerging epidemic hotspots (e.g., Wuhan, Milan, Madrid, New York City, Teheran, Seattle, Detroit and New Orleans) identified temperature, average in-sewer travel time and per-capita water use as key variables. WBE surveillance of populations is shown to be orders of magnitude cheaper and faster than clinical screening, yet cannot fully replace it. Cost savings worldwide for one-time national surveillance campaigns are estimated to be in the million to billion US dollar range (US\$), depending on a nation's population size and number of testing rounds conducted. For resource poor regions and nations, WBE may represent the only viable means of effective surveillance. Important limitations of WBE rest with its inability to identify individuals and to pinpoint their specific locations. Not compensating for temperature effects renders WBE data vulnerable to severe under-/over-estimation of infected cases. Effective surveillance may be envisioned as a two-step process in which WBE serves to identify and enumerate

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infected cases, where after clinical testing then serves to identify infected individuals in WBE-revealed hotspots. Data provided here demonstrate this approach to save money, be broadly applicable worldwide, and potentially aid in precision management of the pandemic, thereby helping to accelerate the global economic recovery that billions of people rely upon for their livelihoods.

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1. Introduction

Months into the pandemic of coronavirus disease 2019 (COVID-19), it remains a global challenge to identify the presence and spread of the SARS-CoV-2 biohazard. The prolonged incubation time and virus shedding from asymptomatic infected cases have allowed the virus to spread quickly and to avoid medical detection and containment. Current estimates of SARS-CoV-2 occurrence are heavily biased toward regions where medical screening of individuals is under way. In contrast, resource-poor regions remain under-tested and disease occurrence underreported. While some countries are now trying to test every individual (e.g., Iceland) to obtain population-wide data, this approach is impractical, slow, and cost-prohibitive for most nations around the world.

Wastewater-based epidemiology (WBE) has been identified as a population-wide infectious disease surveillance tool featuring a proven track record for polio and hepatitis A (Asghar et al., 2014; Hellmér et al., 2014), and holds considerable promise for population-wide surveillance of the COVID-19 pandemic. When first proposed for tracking of SARS-CoV-2, the prevailing scientific opinion was that the virus may be shed into wastewater at insufficiently high rates, and that both the virus itself and its RNA may be too labile to facilitate detection in wastewater. Recent reports of coronavirus shedding in human stool (Gao et al., 2020; Holshue et al., 2020; Jiehao et al., 2020; Tang et al., 2020; Wölfel et al., 2020; Zhang et al., 2020a, 2020b, 2020c, 2020d, 2020e) and three preliminary reports of successful SARS-CoV-2 detection in municipal wastewater from the Netherlands the United States and Australia have dispelled some of these concerns (Ahmed et al., 2020; Lodder and de Roda Husman, 2020; Medema et al., 2020; Wu et al., 2020). Yet, considerable uncertainty remains as to what information may be gleaned from monitoring for SARS-CoV-2 RNA in wastewater and whether a WBE assay, once perfected and shown to be reproducible across different laboratories, will be sensitive enough to inform public health responses. Better population-wide data could aid in reducing the economic damage and social burden placed on populations dealing with stay-at-home ordinances, furlough and involuntary unemployment. At present, public health interventions are implemented with a broad brush; potentially excluding communities that would benefit from them and putting a burden on areas where the virus may currently not pose a threat, thereby rendering hardship-inducing containment measures not only ineffective but also economically and socially disruptive.

The present study combined consideration of economy, scaling, practicability, and data analysis, with a particular focus on wastewater temperature as an underappreciated source of data bias in WBE when performing population-wide screening for SARS-CoV-2.

2. Methodology

2.1. Estimation of initial SARS-CoV-2 loads in wastewater

The SARS-CoV-2 load to municipal wastewater was estimated using excretion rates in human stool recently reported by Zhang et al. (2020e) and Wölfel et al. (2020), and assuming a fecal load in the range of 100–400 g feces/day/person, and a fecal density of 1.06 g/mL (Brown et al., 1996).

2.2. Estimation of COVID-19 persistence in wastewater

The degradation over time of a biomarker of interest present in wastewater can be expected to follow exponential decay, described by the formula as:

$$N(t) = N_0 \left(\frac{1}{2} \right)^{\frac{t}{t_{1/2}}} \quad (1)$$

where $N(t)$ is the quantity that still remains and has not yet decayed after a time (i.e., the amount measured by the sampling campaign); N_0 is the initial quantity of the substance that was excreted and discharged into the wastewater collection system; $t_{1/2}$ is the half-life of the biomarker, and t is the time elapsed between the time of excretion (time = 0) and time of observation/sample collection (time = t).

The adjusted biomarker half-lives were based on the calculated wastewater temperature, a series of initial biomarker half-lives reported at ambient temperatures, and the Arrhenius Equation as shown in Eq. (2):

$$R_2 = R_1 \times Q_{10}^{(T_2 - T_1) / 10 \text{ } ^\circ\text{C}} \quad (2)$$

where R_1 is the initial decay rate, equal to the negative natural log of two divided by the initial reported half-life (Laidler, 1984). When solving for the half-life, Eq. (3) is obtained:

$$t_{1/2, 2} = t_{1/2, 1} \times \frac{\ln(2)}{\ln(2) \times Q_{10}^{(T_2 - T_1) / 10 \text{ } ^\circ\text{C}}} \quad (3)$$

where $t_{1/2, 1}$ is the initial half-life, T_1 is the temperature at which initial half-life was derived, $t_{1/2, 2}$ is the half-life at seasonally- and spatially-

adjusted wastewater temperature calculated in this study, T_2 is the calculated temperature to which initial half-life is adjusted to, and Q_{10} is a factor of temperature-dependent of rate change, ranging between 2 and 3 for most biologic systems (Hart and Halden, 2020a).

2.3. Case study area

This study focused on the City of Tempe, Arizona, USA. The city covers an area of 104 km² and is land-locked by neighboring cities comprising the metropolitan Phoenix area. It has a population of 185,038 according to the 2017 U.S. Census and a density of 1779 people per square kilometer. Land use is predominantly residential, with some industrial and commercial activity.

2.4. Hydraulic model

Data related to the physical layout of the wastewater collection system was obtained from the City of Tempe Water Utilities Department. Wastewater loading was estimated using historic wastewater meter data to derive a per capita wastewater loading rate. Population density estimates were based on Maricopa Association of Governor's Traffic Analysis Zones, with residential wastewater loads assigned

proportionally to population density and maintenance access hole (node) count. Industrial wastewater loads were assigned to the collection system node nearest to the industrial facility, with average flow rates and diurnal curves based on meter data. A previously employed US EPA SWMM model was set up to simulate a 72-hour period representing typical weekday conditions subject to dry weather flows only. No leakage or infiltration was incorporated into the hydraulic model.

2.5. Modeling and numerical analysis

Hydraulic modeling to calculate in-sewer travel time of wastewater in the collection system, volumetric wastewater flow rates, and velocities was performed using the U.S. Environmental Protection Agency's (EPA) SWMM modeling environment (SWMM v.5.1.013; Rossman, 2015). ESRI ArcGIS was used to assign dry-weather flow loading to manholes based on TAZ population densities and the results of the City's metering program. NetSTORM v.2019.06 was used to convert the binary output of SWMM 5.1.013 into time series of flow and velocity at each pipe segment into a format readable by text editors and GIS software (Heineman, 2004). Network Analyst was used in ESRI ArcGIS to perform an accumulation analysis of wastewater travel time from household to outfall over the pipe network. The changing focus of WBE observations in the City of Tempe case study were calculated using the model-simulated travel time from household to outfall, in hours, and the seasonally adjusted half-life in hours.

2.6. Cost analysis for WBE and medical screening of individuals

The per-assay costs of clinical and WBE screening may vary greatly among geospatial regions and around the world due to differing labor costs, safety requirements, existing infrastructure, etc. In order to obtain a more robust and geographically scalable cost estimate, the present analysis only considered assay reagent costs. The key reagents used for clinical and WBE testing, [e.g., real-time quantitative reverse transcription polymerase chain reaction (qRT-PCR) buffers, probes, etc.], are essentially identical (Ahmed et al., 2020; Lodder and de Roda Husman, 2020; Medema et al., 2020; Wu et al., 2020) and were estimated to be on the order of \$10–20 USD with a mean of \$15 USD per test kit, based on market pricing. Future reductions in the per-assay cost would influence the total assay cost but not the relative cost savings that were computed here for clinical screening and WBE using Eqs. (4) and (5):

$$Cost_{P,clinical} = Cost_{reagents} \times P \quad (4)$$

$$Cost_{P,WBE} = Cost_{reagents} \times N_{WWTPs} \quad (5)$$

where $Cost_{P,clinical}$ is the total cost in USD for reagents needed to test a population of the size P , and $Cost_{P,WBE}$ is the total cost in USD for reagents required to screen community wastewater produced by population P in N wastewater treatment plants (N_{WWTPs}).

3. Results and discussion

3.1. Virus occurrence and detectability in wastewater

The SARS-CoV-2 load to municipal wastewater is estimated to be bracketed by the lower and upper bounds estimate of 56.6 million to 11.3 billion viral genomes per infected person per day. This mass load translates into concentrations of 0.15 to 141.5 million viral genomes per liter of wastewater generated in North America and Europe. This is based on the presence of between a reported 600,000 (Zhang et al., 2020e) to 30,000,000 (Wölfel et al., 2020) viral genomes of SARS-CoV-2 per mL of fecal material, and assuming a fecal load of 100–400 g feces/day/person with a density of 1.06 g/mL (Brown et al., 1996). A

further refinement of the lower and upper bounds estimate is desirable and will be informed by future studies providing more comprehensive information on virus shedding by symptomatic and asymptomatic infected individuals.

Assuming a detection limit of 10 coronavirus RNA genomes per mL sewage, and further assuming absence of additional stormwater, commercial, and industrial flow inputs to the sewer system, successful detection of SARS-CoV-2 by qRT-PCR in fully homogenized wastewater will require at worst as much as 0.88% of the population in a monitored sewershed to be infected (1 in 114 individuals) and at best, as few as 0.00005% (1 infected case in about 2 million non-infected individuals). This implies that the practical limit of detection of SARS-CoV-2 in community wastewater is well within the useful range and potentially superior to the alternative approach of randomly testing of 100 to 2 million people to establish presence or absence of symptomatic or asymptomatic cases in a population of interest. The relationship between virus concentration, water use and SARS-CoV-2 detectability is shown in Fig. 1. The plot is useful for determining the theoretical detection limits. However, practical detection limits for the virus may be lower, due to potential loss of qRT-PCR signal in the sewer from virus degradation and RNA loss.

3.2. Impacts of degradation

An assumption of complete virus persistence regardless of travel time in the pipe most certainly is unrealistic. At present, reliable data are lacking for loss of SARS-CoV-2 from in-sewer degradation under any temperature regime. However, a prior study conducted by Gundy et al. (2009) on a different coronavirus strain can serve to provide an approximate benchmark value for virus decay kinetics. According to Eq. (1), and assuming $N_0 = 100$, $N(t) = 0.1$, time $t = 48$ –72 h (Gundy et al., 2009) as well as first-order kinetics, the half-life of SARS-CoV-2 at ambient conditions (20 °C) can be estimated to range between approximately 4.8 and 7.2 h (Table 1). These values are in the same order of magnitude as the typical hydraulic retention times of municipal wastewaters in most sewerage systems around the world. Thus, in most situations in conditions where wastewater flow is at a temperature of 20 °C, at least 25% of the virus load should still remain even in situations where the average in-sewer travel time is long (e.g., 10 h) and the virus stability is relatively low ($t_{0.5} = 4.8$ h).

3.2.1. Impact of seasonal temperature change on SARS-CoV-2/COVID-19 detectability in wastewater

In the absence of seasonal temperature fluctuation, a biomarker discharged into the wastewater collection system at a constant rate would degrade at a rate proportional to its residence time in the system and arrive available for observation at some downstream sampling location at a seasonally invariant rate. However, in actuality, wastewater temperature varies seasonally, and its modulation over the course of a year differs around the world (Hart and Halden, 2020a). Seasonal changes in air and soil temperature affect the transfer of heat between wastewater and the surrounding environment (Fig. 2, panel A). Thus, temperature-adjusted degradation of such a biomarker will not be constant over a year, and instead may vary significantly as shown here for a use case, the city of Tempe, AZ, USA (Fig. 2, panel B). As a result, the same hypothetical constant loading deposited into the sewer upstream will result in different masses available for observation at the downstream monitoring location (Fig. 2, panel C). All else held constant, the degree to which the same seasonality in wastewater temperature will affect downstream observations will increase with increasing in-sewer travel times – i.e., it will be magnified for outfalls serving larger sewersheds, and be more subtle in locations serving smaller sewersheds. We recently showed that failing to account for the role that temperature plays in the degradation of biomarkers can lead to the propagation of error into estimates of upstream discharge, consumption, exposure, and excretion (Hart and Halden, 2020a). The

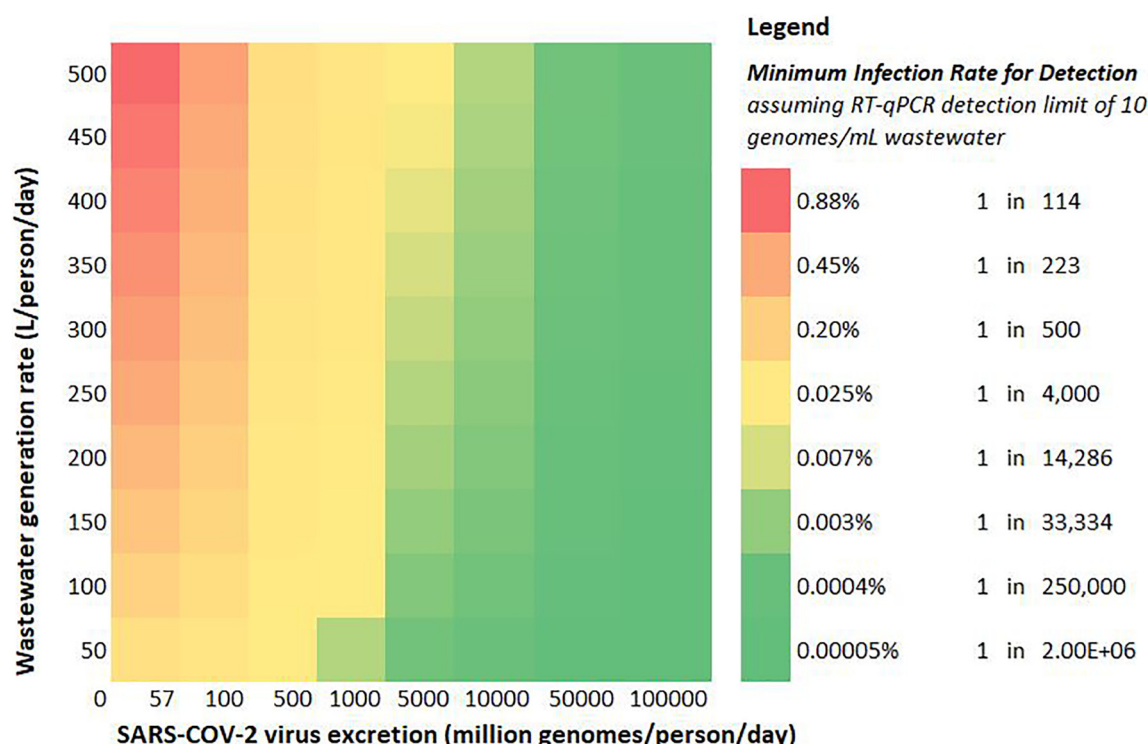


Fig. 1. Under a best-case scenario of no in-sewer signal loss, wastewater generation (50–500 L/person/d) and virus shedding (56.6 million–113.2 billion viromes/d) are important variables determining the detectability in community wastewater of a single infected person among one hundred to two million healthy individuals, assuming homogeneous distribution of cases.

SARS-CoV-2 virus is no exception to this rule. Ignoring temperature effects puts decision-makers at risk of misjudging the public health status and of over- or under-reacting in the selection and implementation of infectious disease control interventions. The effects of temperature adjustment are magnified for longer in-sewer travel times; however, they are evident in some form at every real-world in-sewer travel time (Fig. 2, panel C). WBE studies which do not adjust their monitoring results to temperature will risk significant under- or over-estimation of the true temporal changes occurring in virus shedding within the community (Fig. 2, panel D). Previous studies reporting on the use of WBE for detecting SARS-CoV-2 had very limited surveillance durations (Ahmed et al., 2020; Lodder and de Roda Husman, 2020; Medema et al., 2020; Wu et al., 2020); rendering temperature a marginal factor overall. However, as WBE becomes more common and is being practiced long-term across the changing seasons and differing climate regions, its potentially pronounced effects will have to be taken into consideration in order to obtain robust data and to inform selection of an appropriate public health response.

3.2.2. Wastewater temperature in areas known to be impacted by COVID-19

In prior work, we introduced a deterministic model for computing wastewater temperatures at any location globally (Hart and Halden, 2020a). Here, we applied this model to examine annual changes in

wastewater in locations representing past, present and emerging hot zones of the COVID-19 pandemic; for illustrative purposes, we also include the study use case, the city of Tempe, that thus far has reported relatively fewer cases and a low frequency of detection of SARS-CoV-2 in wastewater (unpublished data). Fig. 3 provides an overview of global locations considered here and the estimated wastewater temperature over the course of the year. Annual temperature swings were most pronounced for the city of Detroit, USA and least pronounced but still notable for the cities of Tempe and New Orleans, USA. Application of the average estimated half-life of 5.95 h calculated in Table 1 and use of the kinetic rate of transformation adjusted according to the Q₁₀ rule (Eqs. (2) and (3)), enabled the calculation of the maximum time a virus load can spend in the sewer line on route to the sampling location before it falls below the estimated limit of detection of qRT PCR. The latter was based conservatively on a loading of 600,000 viral genomes/mL feces (Zhang et al., 2020e) and a wastewater generation rate of 370 L/person/d (Fig. 3). Accordingly, low temperatures of wastewater of the city of Detroit, USA in the winter would enable detection of the virus target even after almost 100 h of in-sewer travel time; however, in the summer the tolerable duration would be reduced down to 20 h. Whereas temperature-related swings in the detectability of SARS-CoV-2 were much less pronounced in Madrid, Spain and Tempe, USA, the relatively higher water temperatures (when compared to Detroit, USA) result in maximum travel times prior to loss of signal of 38 h or less in both locations (Fig. 3).

Table 1
Estimated kinetic parameters of SARS-CoV-2 attenuation in wastewater at ambient temperature.^a

Time to 99.9% reduction (hours)	Half-life, t _{1/2} (hours)	Mean lifetime, τ (hours)	Decay constant, λ
48	4.82	6.95	0.143
72	7.22	10.4	0.096

^a Data entries were informed by Gundy et al., 2009.

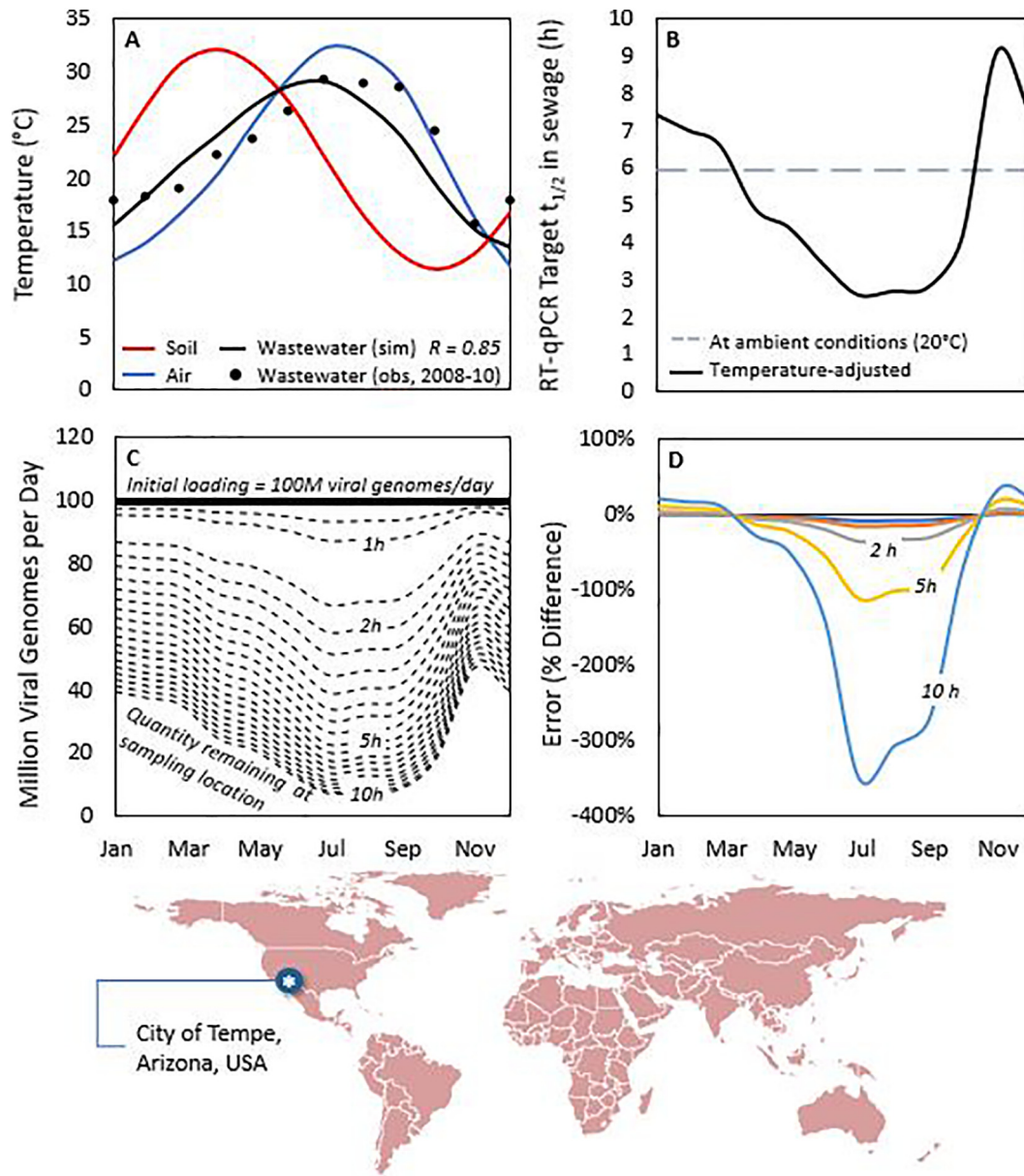


Fig. 2. Seasonal weather conditions influence soil and wastewater temperatures (A), which in turn modulate the in-sewer persistence of SARS-CoV-2 ($t_{1/2}$; B). Assuming shedding of a steady virome load into the sewer (100 M genomes/d), the detectable signal at a city's monitoring location (here Tempe, AZ, USA) will change significantly over the course of a year (C). This is due to temperature-induced variability in the time-to-depletion of the virus below the assumed detection limit of 10 genomes/mL (D).

3.2.3. Impact of seasonal temperature changes on COVID-19 status conclusions

The coming onset of warm weather (April 2020) and increasing wastewater temperatures in the northern hemisphere can result in under-estimates of COVID-19 prevalence in communities. The impact of failing to account for wastewater temperature in back-calculating upstream health metrics increases during the summer and with longer in-sewer travel times (Fig. 4; shown for 0.25–5 h). In Fig. 4, this is illustrated by different loading scenarios and travel times that would be required in order to observe a constant theoretical signal of 100 million virus genomes per unit time passing through the centralized monitoring location in the various COVID-19-impacted cities. A continued observation of the same viral counts in May, June, July, and August as were seen in January, February, and early March would suggest that the case load is stable and the epidemic reasonably managed. However, when taking temperature changes into account, model predictions show that the number of infected individuals actually must have tripled

during that time period (300% increase; Fig. 4; Wuhan and Tempe). This is magnified by the residence time of the virus in the sewer (i.e., the spatial distribution of infected and healthy individuals within a sewershed), which remains a large source of uncertainty in WBE.

3.2.4. Seasonal change in the focus of WBE observations - City of Tempe case study

Despite the relative longevity of the genetic material of SARS-CoV-2 in wastewater and a low estimated limit of detection by qRT PCR, seasonal changes in wastewater temperature result in a changing population focus for WBE observations over the course of a year. Using the City of Tempe as a case study, the pronounced difference in the composition of a sewershed outfall's sample makeup during the winter and summer months is further illustrated in Fig. 5. Here, the model-simulated in-sewer travel time is mapped to the nearest building footprint using an actual, as-built, city sewer network. Modeling results show that, during winter months, the sewershed is captured more

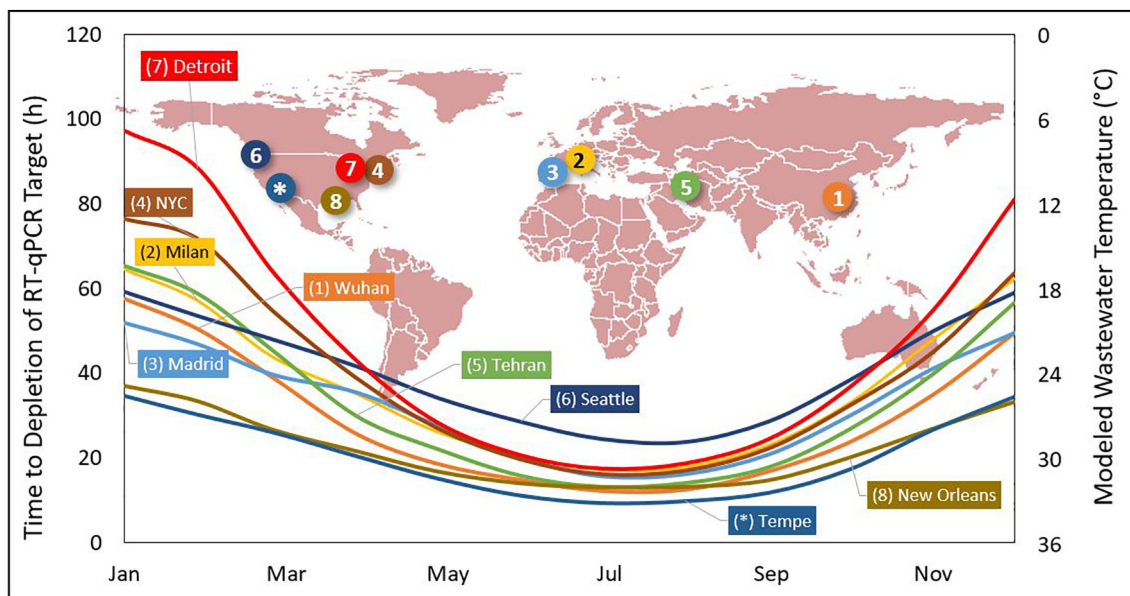


Fig. 3. Annual change of the in-sewer time to depletion of SARS-CoV-2 computed for 8 cities impacted by the COVID-19 pandemic and for the present use case, the city of Tempe, Arizona (USA).

evenly and the concentrations of SARS-CoV-2 sampled at the basin's outfall represent more closely the COVID-19 status of the sewershed's population as a whole. During the summer months, wastewater

sampling at the outfall will reflect the health status of individuals living closer to the WBE sampling location, and the measurements marginalize or do not capture at all the health status of household members

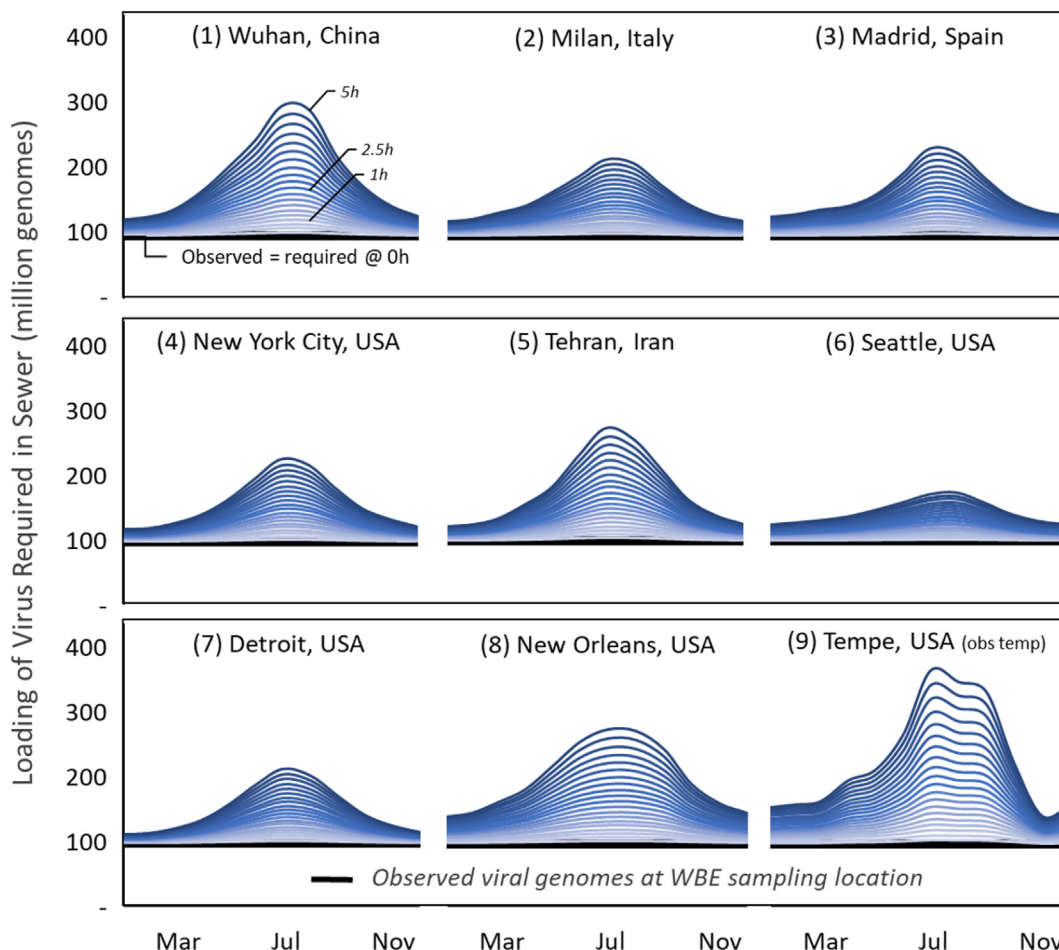


Fig. 4. Model output, illustrating how a constant signal observed at the intake of a given city's wastewater treatment plant (solid black line) may result from a multitude of different combinations of virus loadings, depending on seasonal weather conditions that dictate in-sewer decay of the qRT PCR signal.

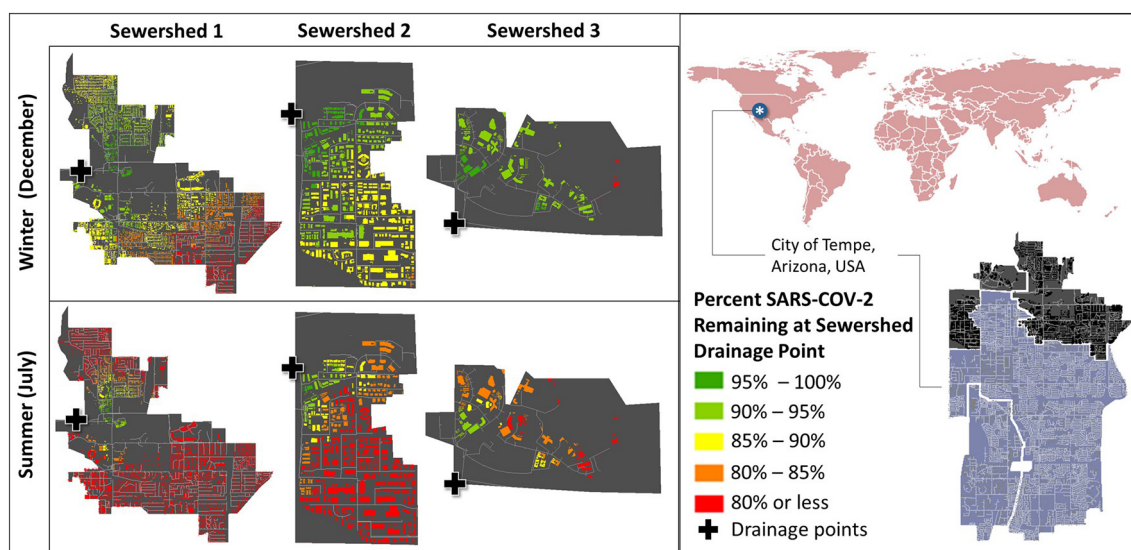


Fig. 5. Tempe, AZ undergoes extreme seasonal temperature changes which are predicted to impact SARS-CoV-2 detectability as illustrated by computer simulations. The city has been monitoring wastewater for opioids since May 2018, first in 3 and currently in 5 areas, and recently started monitoring for COVID-19 with the intent of adding this new data source to an existing public health online dashboard to which wastewater analysis data get posted in real-time (<https://arcg.is/ey0Ha>).

residing near the sewershed's edges. This phenomenon of seasonal differences influencing how far WBE "can see up the sewer line" and how the demographics of the surveilled population changes as a result of contracting and expanding effective area observed had been described previously for chemical markers by our team (Hart and Halden, 2020a, 2020b).

3.3. Cost and practicability considerations of clinical testing and WBE

Even in countries like Germany, where the testing capacity is highest in Europe at about 100,000 clinical assays per day (NYT, 2020), almost 3 months of non-stop testing would be required to assess the infection status of the entire 83 million population just once. This implies that comprehensive screening of a nation's population using individual test kits is not only expensive (approximately \$1.25 billion USD for Germany for assay reagents only) but also impractically slow (3 months, during which major changes can occur in the prevalence of the virus in the community). In contrast, all of Germany's 9636 wastewater treatment plants could easily be sampled and analyzed within 24 to 48 h, due to the country's favorable transportation and testing infrastructure, at a cost for reagents alone of only \$145,000 USD. In this case, the cost for WBE surveillance reagents would constitute only 0.014% of those required for clinical testing of individuals. This implies that testing this nation's wastewater millions of times over again would still be cheaper than a single screening of all people individually. For both speed and economy, these order-of-magnitude cost estimates heavily favor WBE over clinical screening for population health assessment. Similarly, about 70% of the US population could be screened for SARS-CoV-2 community spread by analyzing in 48 h all 15,014 wastewater treatment plants at an estimated reagent cost of approximately \$225,000 USD. The US currently still has limited clinical testing capacity, rendering individual screening of the 330 million population impractical. In addition, this approach would be too slow and cost-prohibitive, with clinical screening of all Americans leading to reagent costs alone of some \$3.5 billion USD per sampling event. Even if the cost of reagents for clinical screening could be reduced by 99% in the future (e.g., through the introduction of paper-based assays) (Mao et al., 2020), the associated costs and logistical challenges still would render this approach questionable and unresponsive to the need of retesting a population to learn about new and repeated infections.

For rapidly and repeatedly obtaining a health profile of billions of people around the world, the economy, speed and versatility of the

WBE approach thus is difficult to match or surpass. We estimate that WBE today could reach some 2.1 billion people around the world whose household is connected to one of the approximately 105,600 wastewater treatment plants operated globally. Several nations, including various European countries (SCORE, 2017), Australia (Lai et al., 2018), Israel (Asghar et al., 2014), and China (Feng et al., 2018), already have made strategic investments into WBE at the national level. Whereas the US is home to the largest national and international WBE network and sample repository, the Human Health Observatory (HHO) at Arizona State University, this shared resource (Halden et al., 2019; Venkatesan et al., 2015; Venkatesan and Halden, 2014; Bowes and Halden, 2019) was created over the course of a dozen years primarily with discretionary funds from philanthropists and support from partnering municipalities (Gushgari et al., 2018, 2019; Chen et al., 2019; Driver et al., 2020). Among the latter, the city of Tempe, AZ stands out as an innovator in WBE data communication, by immediately releasing obtained wastewater data on locally consumed licit and illicit opioids via an online dashboard to inform the public, emergency response teams, and policy makers (ASU-Tempe, 2020).

As is true for any modeling study, output data are only as good as the input information provided. For the present work, a number of areas would benefit from additional experiments and the parameterization of phenomena important for understanding virus detectability. Improvements would be welcome in lowering the detection limit and in increasing the precision of quantitative data, possibly achievable via use of digital PCR (Majumdar et al., 2015). Whereas processing of larger sample volumes and more effective concentration of virus particles and viral RNA may help to lower method detection limits, there also is a desire to keep required samples sizes low enough to facilitate economic shipping between sampling location and the analytical laboratory.

Finally, it is important to note that the simulations conducted here are exclusively directed at the detection of the occurrence of the virus and the number of virus particles per unit wastewater. The data provided here should not be interpreted as providing information on the presence of intact, infective virus particles (Casanova and Weaver, 2015; Casanova et al., 2009). Data on the infectivity of sewage-borne SARS-CoV-2 is urgently needed but difficult to obtain, due to the temporary closure of many research laboratories and the need for biosafety level certification in excess of Level 2 to conduct this type of work. Such work also should address a study on the decay and detectability of SARS-CoV-2 as a function of temperature.

4. Conclusions

This computational modeling study and cost analysis served to identify WBE as a rapid, inexpensive and potentially robust tool for tracking SARS-CoV-2/COVID-19. Effective use of this emerging surveillance tool will require the consideration of temperature effects in order to obtain robust, informative data. Whereas WBE cannot replace clinical testing, it can serve to alert emergency response teams to the presence of infected individuals in towns, cities and specific drainage areas (sub-sewersheds) of large metropolitan areas down to the neighborhood and building complex level. The feasibility of performing longitudinal monitoring of wastewater at the city-area/neighborhood level already has been demonstrated in the city that served as the use case of this study, Tempe, AZ, where SARS-CoV-2 recently was added to a spectrum of public health indicator that have been tracked continuously since May 2018. To accelerate the global economic recovery, it is desirable to implement restrictions to people's mobility and livelihoods only in locales where these are needed. WBE is well positioned to inform this local decision-making process. WBE also appears to constitute the only viable means of enabling large-scale population-wide testing globally, particularly in resource poor regions. Since effective use of large-scale WBE requires access to wastewater that is centrally collected, composited and treated, the global use of WBE relying on sampling of wastewater treatment plants currently is restricted to about 2.1 billion people or 27% of the global population. Billions of additional people could benefit from human waste analysis by integrating sampling of latrines into global health surveillance. However, the required effort would be disproportionately larger and the number of people reflected in each sample relatively low. Yet, if only 1% of the resources currently allocated for clinical testing were diverted to WBE, significant cost savings could be realized, vulnerable populations could be protected more effectively, and economic recovery could be balanced locally more selectively with the need for containing community spread of the new coronavirus.

CRedit authorship contribution statement

Olga E. Hart: Conceptualization, Methodology, Formal analysis, Visualization, Writing - original draft, Writing - review & editing. **Rolf U. Halden:** Conceptualization, Data curation, Formal analysis, Writing - original draft, Writing - review & editing.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Dr. Halden is co-founder of AquaVitas, LLC, an Arizona State University (ASU) startup company that works in the intellectual space touched upon by this study. Dr. Halden further is founder of ASU Foundation's OneWaterOneHealth, a nonprofit project providing wastewater-based health assessments to underserved US communities.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.scitotenv.2020.138875>.

References

- Ahmeda, W., Angel, N., Edson, J., Bibby, K., Bivins, A., O'Brien, J.W., Choi, P.M., Kitajima, M., Simpson, S.L., Li, J., Tschärke, B., Verhagen, R., Smith, W.J.M., Zaugg, J., Dierens, L., Hugenholtz, P., Thomas, K.V., Mueller, J.F., 2020. Science of the Total Environment (In Press).
- Asghar, H., Diop, O.M., Weldegebriel, G., Malik, F., Shetty, S., Bassioni, L. El, Akande, A.O., Maamoun, E. Al, Zaidi, S., Adeniji, A.J., Burns, C.C., Deshpande, J., Oberste, M.S., Lowther, S.A., 2014. Environmental surveillance for polioviruses in the global polio eradication initiative. *J. Infect. Dis.* <https://doi.org/10.1093/infdis/jiu384>.
- ASU-Tempe, Arizona State University – City of Tempe Academic-Municipal Partnership, 2020. World's first online dashboard for immediate public release of information collected by wastewater-based epidemiology. Story Map (<https://arcg.is/PKWuz>) and Opioid Dashboard <https://arcg.is/ey0Ha>.
- Bowes, D.A., Halden, R.U., 2019. Theoretical evaluation of using wastewater-based epidemiology to assess the nutritional status of human populations. *Current Opinion in Environmental Science & Health* 9, 58–63. <https://doi.org/10.1016/j.coesh.2019.05.001>.
- Brown, D.M., Butler, D., Orman, N.R., Davies, J.W., 1996. Gross solids transport in small diameter sewers. *Water Sci. Technol.* 33 (9), 25–30.
- Casanova, L.M., Weaver, S.R., 2015. Inactivation of an enveloped surrogate virus in human sewage. *Environmental Science and Technology Lett* 2, 76–78.
- Casanova, L.M., Rutala, W.A., Weber, D.J., Sobsey, M.D., 2009. Survival of surrogate coronaviruses in water. *Water Res.* 43, 1893–1898.
- Chen, J., Venkatesan, A., Halden, R.U., 2019. Alcohol and nicotine consumption trends in three U.S. communities determined by wastewater-based epidemiology. *Sci. Total Environ.* 656, 174–183.
- Driver, E.M., Gushgari, A., Chen, J., Halden, R.U., 2020. Longitudinal study of alcohol, nicotine, and caffeine consumption on a public university campus via wastewater-based epidemiology. *Sci. Total Environ.* 727, 138492.
- Feng, L., Zhang, W., Li, X., 2018. Monitoring of regional drug abuse through wastewater-based epidemiology—a critical review. *Science China Earth Sciences* 61 (3), 239–255.
- Gao, Q.Y., Chen, Y.X., Fang, J.Y., 2020. 2019 novel coronavirus infection and gastrointestinal tract. *J. Dig. Dis.* <https://doi.org/10.1111/1751-2980.12851>.
- Gundy, P.M., Gerba, C.P., Pepper, I.L., 2009. Survival of coronaviruses in water and wastewater. *Food and Environmental Virology* 1 (1), 10.
- Gushgari, A.J., Driver, E.M., Steele, J.C., Halden, R.U., 2018. Tracking narcotics consumption at a Southwestern U.S. university campus via wastewater-based epidemiology. *J. Hazard. Mater.* 359, 437–444. <https://doi.org/10.1016/j.jhazmat.2018.07.073>.
- Gushgari, A.J., Venkatesan, A.K., Chen, J., Steele, J.C., Halden, R.U., 2019. Long-term tracking of opioid consumption in two United States cities using wastewater-based epidemiology. *Water Res.* 161, 171–180. <https://doi.org/10.1016/j.watres.2019.06.003>.
- Halden, R.U., Terlinden, E., Kraberger, S., Scotch, M., Steele, J., Varsani, A., 2019. Tracking harmful chemicals and pathogens using the Human Health Observatory at ASU. *Online Journal of Public Health Informatics* 11 (1), e369. <https://doi.org/10.5210/ojphi.v11i1.9843>.
- Hart, O.E., Halden, R.U., 2020a. Modeling wastewater temperature and attenuation of sewage-borne biomarkers globally. *Water Res.* 172. <https://doi.org/10.1016/j.watres.2020.115473>.
- Hart, O. E. and Halden R.U.* (2020b). Simulated 2017 nationwide sampling at 13,940 major U.S. sewage treatment plants to assess seasonal population bias in wastewater-based epidemiology. *Sci. Total Environ.* 727, 138406.
- Heineman, M. C. (2004). NetSTORM-A computer program for rainfall-runoff simulation and precipitation analysis. In *Critical Transitions in Water and Environmental Resources Management* (pp. 1–14). Software available at: <http://www.dynsystem.com/netstorm/>.
- Hellmér, M., Paxéus, N., Magnius, L., Enache, L., Arnholm, B., Johansson, A., Bergström, T., Norder, H., 2014. Detection of pathogenic viruses in sewage provided early warnings of hepatitis A virus and norovirus outbreaks. *Appl. Environ. Microbiol.* <https://doi.org/10.1128/AEM.01981-14>.
- Holshue, M.L., DeBolt, C., Lindquist, S., Lofy, K.H., Wiesman, J., Bruce, H., Spitters, C., Ericson, K., Wilkerson, S., Tural, A., Diaz, G., Cohn, A., Fox, L.A., Patel, A., Gerber, S.I., Kim, L., Tong, S., Lu, X., Lindstrom, S., Pallansch, M.A., Weldon, W.C., Biggs, H.M., Uyeki, T.M., Pillai, S.K., 2020. First case of 2019 novel coronavirus in the United States. *N. Engl. J. Med.* <https://doi.org/10.1056/NEJMoa2001191>.
- Jiehao, C., Jing, X., Daojiong, L., Lei, X., Zhenghai, Q., Yuehua, Z., Hua, Z., Xiangshi, W., Yanling, G., Aimei, X., He, T., Hailing, C., Chuning, W., Jingjing, L., Jianshe, W., Mei, Z., Children, N., Women, H., Central, S., Zeng, M., 2020. A case series of children with 2019 novel coronavirus infection: clinical and epidemiological features. *Clin. Infect. Dis.* <https://doi.org/10.1093/cid/ciaa198> [Epub ahead of print].
- Lai, F.Y., Gartner, C., Hall, W., Carter, S., O'Brien, J., Tschärke, B.J., Been, F., Gerber, C., White, J., Thai, P., 2018. Measuring spatial and temporal trends of nicotine and alcohol consumption in Australia using wastewater-based epidemiology. *Addiction* 113 (6), 1127–1136.
- Laidler, K.J., 1984. The development of the Arrhenius equation. *J. Chem. Educ.* 61 (6), 494.
- Lodder, W., de Roda Husman, A., 2020. SARS-CoV-2 in wastewater: potential health risk, but also data source. *Lancet Gastroenterol. Hepatol.* 1253, 30087.
- Majumdar, N., Wessel, T., Marks, J., 2015. Digital PCR modeling for maximal sensitivity, dynamic range and measurement precision. *PLoS One* 10 (3), e0118833 (PMC4373789).
- Mao, K., Zhang, H., Yang, Z., 2020. Can a paper-based device trace COVID-19 sources with wastewater-based epidemiology? *Environ. Sci. Technol.* 54 (7).
- Medema, G., Heijnen, L., Elsinga, G., Italiaander, R., 2020. Presence of SARS-Coronavirus-2 in sewage. *medRxiv*. <https://doi.org/10.1101/2020.03.29.20045880>.
- New York Times, 2020. <https://nyti.ms/3epj26y>.

- Rossman, L.A., 2015. *Storm Water Management Model User's Manual Version 5.1*. Office of Research and Development. Water Supply and Water Resources Division. US Environmental Protection Agency (EPA/600/R-14/413b).
- SCORE - Sewage Analysis CORE group Europe, 2017. *COST Action ES1307*.
- Tang, A., Tong, Z., Wang, H., Dai, Y., Li, K., Liu, J., Wu, W., Yuan, C., Yu, M., Li, P., Yan, J., 2020. Detection of novel coronavirus by RT-PCR in stool specimen from asymptomatic child, China. *Emerg. Infect. Dis.* <https://doi.org/10.3201/eid2606.200301>.
- Venkatesan, A.K., Halden, R.U., 2014. Wastewater treatment plants as chemical observatories to forecast ecological and human health risks of manmade chemicals. *Sci. Rep.* 4, 3731. <https://doi.org/10.1038/srep03731>.
- Venkatesan, A.K., Done, H.Y., Halden, R.U., 2015. United States National Sewage Sludge Repository at Arizona State University – a new resource and research tool for environmental scientists, engineers, and epidemiologists. *Environ. Sci. Pollut. Res. Int.* 22 (3), 1577–1586. <https://doi.org/10.1007/s11356-014-2961-1>.
- Fuqing Wu, Amy Xiao, Jianbo Zhang, Xiaoqiong Gu, Wei Lin Lee, Kathryn Kauffman, William Hanage, Mariana Matus, Newsha Ghaeli, Noriko Endo, Claire Duvallet, Katya Moniz, Timothy Erickson, Peter Chai, Janelle Thompson, Eric Alm. SARS-CoV-2 titers in wastewater are higher than expected from clinically confirmed cases. doi: <https://doi.org/10.1101/2020.04.05.20051540>.
- Wölfel, R., Corman, V.M., Guggemos, W., Seilmaier, M., Zange, S., Müller, M.A., Niemeyer, D., Jones, T.C., Vollmar, P., Rothe, C., Hoelscher, M., Bleicker, T., Brünink, S., Schneider, J., Ehmann, R., Zwirgmaier, K., Drosten, C., Wendtner, C., 2020. Virological assessment of hospitalized patients with COVID-2019. *Nature*, 1–10 <https://doi.org/10.1038/s41586-020-2196-x>.
- Zhang, J.C., Wang, S. Bin, Xue, Y.D., 2020a. Fecal specimen diagnosis 2019 novel coronavirus-infected pneumonia. *J. Med. Virol.* <https://doi.org/10.1002/jmv.25742>.
- Zhang, N., Gong, Y., Meng, F., Bi, Y., Yang, P., Wang, F., 2020b. *Virus Shedding Patterns in Nasopharyngeal and Fecal Specimens of COVID-19 Patients*. *Infectious Diseases (except HIV/AIDS)*.
- Zhang, W., Du, R.H., Li, B., Zheng, X.S., Yang, X. Lou, Hu, B., Wang, Y.Y., Xiao, G.F., Yan, B., Shi, Z.L., Zhou, P., 2020c. Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerg. Microbes Infect.* <https://doi.org/10.1080/22221751.2020.1729071>.
- Zhang, Y., Chen, H., Zhu, S., 2020d. Isolation of 2019-nCoV From a Stool Specimen of a Laboratory Confirmed Case of the Coronavirus Disease 2019 (COVID-19). 2 pp. 123–124.
- Zhang, N., Gong, Y., Meng, F., Bi, Y., Yang, P., Wang, F., 2020e. Virus Shedding Patterns in Nasopharyngeal and Fecal Specimens of COVID-19 Patients. medRxiv <https://doi.org/10.1101/2020.03.28.20043059> press.