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Model-Based Evaluation of Reduction Strategies for Micropollutants from Wastewater Treatment Plants in Complex River Networks

CHRISTOPH ORT,*,†,‡ JULIANE HOLLENDER,† MICHAEL SCHAERER,§ AND HANSRUEDI SIEGRIST†

Eawag, Swiss Federal Institute of Aquatic Science and Technology, CH-8600 Dübendorf, Switzerland, The University of Queensland, Advanced Water Management Centre (AWMC), Qld 4072, Australia, and Federal Office for the Environment, Water Division, CH-3003 Bern, Switzerland

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A model based on graph theory was developed to efficiently evaluate the impact of the effluent from 742 wastewater treatment plants (WWTPs) on micropollutant loading throughout all river catchments in Switzerland. Model results agree well with measured loads for 12 compounds in river water samples, revealing mean predictive accuracy factors between 0.8 and 3.4. Subsequently, pollutant concentrations were predicted for river sections downstream from 543 WWTPs where hydrological information was available, and compared with recent recommendations for water quality criteria. At base flow conditions, carbamazepine concentrations (parent compound only) are ubiquitously below a water quality criterion of 0.5 μg L^{-1}. In contrast, the sum of diclofenac and its metabolites is expected to exceed the corresponding water quality criterion of 0.1 μg L^{-1} in 224 river sections. If diclofenac cannot be eliminated at the source, the model suggests a directed upgrade of 173 WWTPs to meet the condition that concentrations are never to exceed this water quality criterion.

Introduction

Public awareness of and scientific interest in aquatic micropollutants are increasing. Micropollutant concentrations have been reported for thousands of water samples, in part due to the development and constant improvement of chemical analytical methods (*1*). Examples include the effect of endocrine disrupting compounds on fish (*2*) and the occurrence of pharmaceutical residues in drinking water (*3*). Future challenges have been addressed by several authors, and are summarized in a review by Schwarzenbach et al. (*4*). An intensively discussed issue is the development and application of more efficient and cost-effective wastewater treatment steps (*5, 6*). Technologies such as advanced oxidation or sorption to activated carbon, which effectively remove micropollutants, may soon become available in wastewater treatment plants (WWTPs) at full scale. Additionally, a growing number of water quality criteria have recently been recommended for several compounds (*7*). Therefore, the Swiss Federal Office for the Environment initiated an interdisciplinary project to formulate an optimized strategy for upgrading WWTPs. To allocate resources appropriately in the future, the current exposure of Swiss surface waters to micropollutants from WWTPs needs to be assessed: pollutant concentrations can either be measured or estimated with a model. Advantages and disadvantages of these two approaches are discussed below.

Despite the absence of legally binding numeric water quality criteria, many environmental protection agencies determine and publish micropollutant concentrations in water bodies in their custody. A meaningful comparison of concentrations reported by different authorities can be difficult, because values are often averaged over different periods or even locations and precise conditions at the date of sampling are rarely provided. Flow rates, for example, are essential to calculate loads. Combined with the number of inhabitants in the catchment, loads allow for a more sound interpretation of measured data: per capita loads can be meaningfully compared with loads calculated from consumption data and can be transferred to other regions because loads generally vary less than concentrations. Unfortunately, sporadic measurements may not reflect long-term conditions (*8*) and operating a systematic monitoring scheme, to collect representative samples at sufficiently high spatial and temporal resolution (*9*), is very costly. Nevertheless, measurements are indispensable, since they provide the only means of assessing the real situation, at least for a specific point in time.

To overcome some of the limitations related to sampling, models can be applied to perform risk assessments. Basically, two categories exist: multimedia models such as EUSES, and in-stream water quality models such as GREAT-ER. Multimedia models, aimed to determine the global risk among environmental compartments, are not designed to undertake site-specific risk assessments (*10*). To identify hotspots in a river catchment, different in-stream water quality models for down-the-drain chemicals are proposed. Typically, the initial model setup requires large amounts of data and skilled practitioners (*8*). Hence, these models are usually only applied to single, validated catchments and not to whole countries with large, complex river networks. Approaches to reduce the data demand were suggested (*11, 12*) but not validated for micropollutants across catchments. Additionally, they describe the present situation but do not allow for a fast and flexible formulation of user-defined algorithms to calculate scenarios.

Therefore, we present an elementary modeling approach applying graph theory. The model was set up with the following objectives: predict realistic micropollutant loads from WWTPs in rivers and screen for hotspot concentrations across catchments at a national scale; use a minimum of required input data (existing digital river network, location of WWTPs' discharge points, consumption data, human metabolism and elimination in WWTPs); and program algorithms to determine optimized reduction strategies. The model was validated with site-specific measurements.

Material and Methods

Model Setup. The model includes all of the 742 WWTPs in Switzerland, each with a design capacity of more than 500 population equivalents (PE), serving over 97% of the population. WWTPs discharge to surface waters and are thus quasi-

* Corresponding author e-mail: c.ort@awmc.uq.edu.au; phone +61 (0)7 3346 6252; fax +61 (0)7 3365 4726.
† Eawag, Swiss Federal Institute of Aquatic Science and Technology.
‡ The University of Queensland.
§ Federal Office for the Environment.

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connected via rivers and lakes. Therefore, the river network exposed to treated wastewater can be captured by a directed graph. A didactical example is given in SI 1. The network was calculated according to Cormen (*13*) by the matrix operation

$$(T_{ij}) = (I - W)^{-1} \quad (1)$$

where T_{ij} denotes the topology-matrix, I is the identity-matrix, and W is the adjacency-matrix. All calculations are implemented in the software R (*14*).

Input Data and Transformation Processes. The only catchment-related input is the population each WWTP serves. These data were updated for all WWTPs in Switzerland in 2006 (*15*). The model also requires substance-specific inputs on consumption, human metabolism rates, and WWTP removal rates for each compound under investigation. Official national sales data were obtained from IMS Health Ltd. covering all relevant distribution channels in Switzerland. As an approximation in the model, the annual consumption is evenly distributed over the population and throughout all days of the year. Human metabolism and conventional WWTP removal rates were accounted for with transfer coefficients by subtracting a percentage in the mass flux calculations.

Fate in Natural Water Bodies. The half-lives of many pharmaceutically active compounds are on the same order of magnitude or larger than the maximum residence time in Swiss rivers. All Swiss rivers have a residence time of less than one day, defined from their formation until they reach a reservoir (lake) or leave the country. Hence, it is assumed that no significant degradation occurs in rivers, and substances are modeled to be recalcitrant within these system boundaries. However, degradation processes can lead to complete elimination in lakes due to considerably longer residence times. For example diclofenac is known to be prone to photodegradation (*16*). Therefore, the model allows for predicting compounds that either are or are not eliminated in lakes. Since the focus was on soluble, polar compounds, sorption to sediments was neglected as a loss process.

Daily Mass Fluxes. The average daily load of a substance expected in a river section downstream from a WWTP can be calculated with the previously described input data and model structure. It is the sum of all loads from WWTPs contributing from upstream to this river section:

$$L(S)_{\text{river catchment WWTP}_j} = \frac{1000}{365} \times \sum_i \left[\frac{C_{CH}}{P_{CH}} \times (p + m)\right] \cdot \bar{P}_{WWTP} \cdot (1-\bar{e}) \cdot (T_{ij}) \quad (2)$$

where $L(S)$ is the average daily load of substance S [g d^{-1}]; C_{CH} is the annual national consumption of substance S [kg a^{-1}]; P_{CH} is total population in Switzerland (7.459 million); p is the fraction of parent compound excreted and discharged to sewers; m is the fraction of known metabolites, given as toxicity equivalents of the parent compound as calculated by Lienert et al. (*17*); $\bar{P}_{WWTP}$ is the population connected to each WWTP [number of inhabitants], $\bar{e}$ is the fraction of substance S eliminated in WWTPs; and T_{ij} is derived from eq 1. As a first step, modeled pollutant loads were compared with loads determined from environmental observations.

Monitoring Study. In Switzerland, no systematic micropollutant monitoring program exists and studies of local authorities often focus on larger rivers. Therefore, we selected nine locations in smaller creeks and medium-sized rivers across the country to compare model predictions with measurements (see Figure 1). The main criteria for the sampling locations were that river catchments contain at least one WWTP with a design capacity larger than 500 PE and a well-maintained gauging station was nearby to calculate

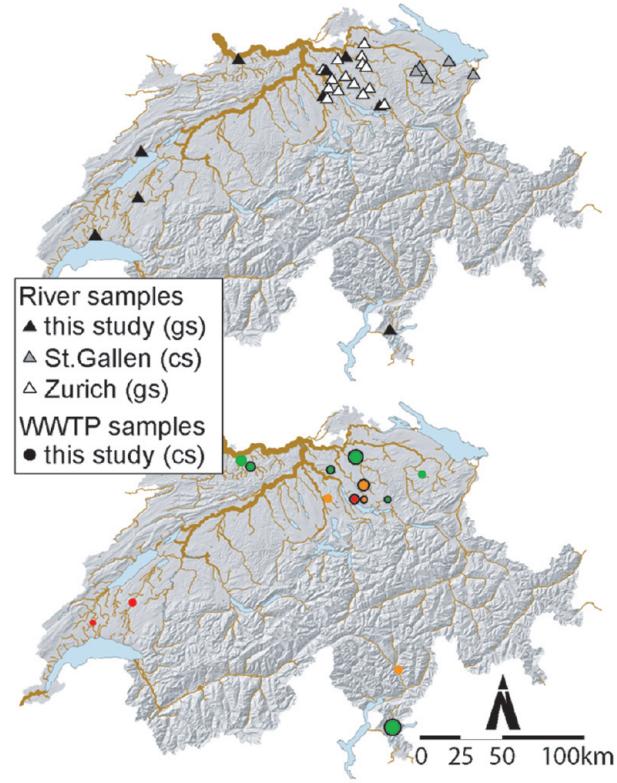

FIGURE 1. Triangles: Sampling locations in rivers; catchment sizes range from 5,000 to 410,000 inhabitants; gs = grab samples, cs = composite samples. Circles: selected WWTPs covering different categories; red = BOD removal only, orange = nitrifying, green = nutrient removal, black border = filtration, size of circles proportional to population served (min. 6,000 to max. 19,000). Maps reproduced by permission of swisstopo (BA081497).

loads. Samples were collected in August and September 2007 (sampling and chemical analyses are described in SI 2 and a list of compounds can be found in SI 3). Additional measurements for carbamazepine and diclofenac were provided by the local authorities of the Cantons Zurich and St. Gallen. Their sampling campaigns took place in November 2004 and April 2005 respectively (see SI 2 for more information). The number of inhabitants in all investigated river catchments varied between 5,000 and 410,000. Additionally, samples from 14 WWTPs were collected to determine per capita load variations in influents and effluents. Furthermore, they allowed for plausibility checks if measured loads in rivers were questionably high or low.

Pollutant Concentrations. If model predictions for pollutant loads, calculated as described before, do not significantly deviate from measured data, predicted environmental concentrations (PEC) can be calculated. To this end, daily loads were divided by daily flows in the river. Base flow conditions ($Q_{95\%}$) were used to account for minimum dilution. The $Q_{95\%}$ is the flow reached or exceeded in 95% of the time annually, in Switzerland averaged over a ten-year period. Where no measurements for $Q_{95\%}$ were available, values were interpolated (see SI 4). This procedure led to $Q_{95\%}$ values for river sections downstream from 543 WWTPs out of the 660 that discharge to rivers. The 117 WWTPs with no estimate for $Q_{95\%}$ are all small, treating only 5% of the total PE in Switzerland. Their pollutant loads, as well as the ones from the 82 WWTPs discharging directly to lakes, are included in the calculations, but concentrations could not be determined directly downstream from these WWTPs. Predicted envi-

ronmental concentrations were then compared with published water quality criteria (WQC).

Reduction Strategies. Depending on the objective, various reduction strategies can be formulated. The two main strategies based on water quality and load reduction and a combination thereof are presented subsequently.

1. Water Quality. The goal of this strategy is to avoid any exceedance of a WQC in the whole river network by upgrading selected WWTPs. An optimizing algorithm was introduced in the model, finding the smallest number of WWTPs for which an upgrade would be necessary. The algorithm starts at the first WWTP on a river and checks whether the WQC is exceeded in the river downstream of this WWTP or not. If yes, this WWTP will be upgraded, resulting in a higher elimination of the compound under consideration at this WWTP. The algorithm repeats this procedure downstream for all rivers. Elimination rates of 95% are assumed for upgraded WWTPs, corresponding to the treatment efficiency of ozonation or activated carbon (*18, 19*).

2. Load Reduction. The goal of the second strategy is to efficiently achieve a substantial load reduction. The selection of WWTPs to be upgraded is based solely on their size. It is independent of location and does not consider pollutant concentrations in rivers. With this preselection, the effect on water quality improvement was calculated.

3. Combination. A combination of the two strategies focuses in a first step on upgrading the largest WWTPs, each with more than 100,000 PE, and then applies the "Water Quality" strategy.

Uncertainty Propagation. Model parameters are subject to geographic and temporal variation. The "true" values and their distributions are largely unknown. Subsequently we consider this as "uncertainty". Its effect on the final result was estimated by means of a Monte Carlo simulation.

In view of observed load variations in WWTP influents (measurements at 14 WWTPs, data not shown) an uncertainty range of ±50% was derived and assumed to be uniformly distributed: uniform(−0.5, 0.5). This covers the variable consumption and human excretion. In each model run, an individual random value from this uniform distribution is assigned to each WWTP and added to the average influent load. Example: if a random value of +32% was sampled for $WWTP_1$, its influent load for this run would be 132% of the average influent load. In the same run, an independent random value will be assigned to $WWTP_2$, for example −15%, etc. With this procedure and due to the large number of WWTPs the sum of influent loads over all WWTPs remains constant in one run but reflects a possibly uneven distribution of the national consumption among the different catchments. In a similar way, varying elimination rates in WWTPs were considered with ±20%: uniform(−0.2, 0.2). The uncertainty from chemical analyses was accounted for with another ±20%: uniform(−0.2, 0.2).

For the uncertainty of $Q_{95\%}$ an estimate was made with independent measurements: according to Figure SI 4.2 a range of ±70% was derived for the category of small creeks ($Q_{95\%} < 60$ L s^{-1}), ±50% for medium-sized rivers (60 L s^{-1} < $Q_{95\%} < 600$ L s^{-1}), and ±30% for larger rivers ($Q_{95\%} > 600$ L s^{-1}). While it is justified to assume that individual uncertainty factors for calculating loads are independent within one model run, this does not hold true for $Q_{95\%}$: a lower value upstream also implies a lower value downstream to ensure consistency within catchments. The complete sampling procedure for uncertainty values used in the Monte Carlo simulation is outlined in SI 5.

Results and Discussion

Daily Mass Fluxes. Average daily mass fluxes were calculated for carbamazepine and diclofenac for all river sections in Switzerland. Model input values are listed in Table 1. The comparison of predicted versus measured loads is plotted in Figure 2.

TABLE 1. Model Input Parameters and Expected Per Capita Loads Per Day

	unit	carbamazepine	diclofenac
sales data Switzerland[a]	kg a^{-1}	4400	4000
parent compound unchanged to sewer (*17*)	%	10[b]	16
known metabolites (*17*)	%	26[c] (41)[d]	20[c] (65)[d]
average elimination WWTP (*20*)	%	0	25
elimination in natural water bodies		none	full elimination in lakes[g]
expected loads			
influent WWTP	μg c^{-1} d^{-1}	160[e] 580[f]	240[e] 530[f]
effluent WWTP	μg c^{-1} d^{-1}	160[e] 580[f]	180[e] 400[f]

[a] Average from the years 2000 and 2004 (sales data obtained from IMS Health Ltd.); individual annual sales data only deviate by ±10% of the average used. [b] Fraction in feces (8%) was estimated from measured WWTP influents, because in Lienert et al. (*17*) only the fraction in urine was reported (2%). [c] As parent compound toxicity equivalents. [d] Approximate percentage of administered mass. [e] Only parent compound. [f] Parent compound plus toxicity equivalents from known metabolites. [g] Buser et al. (*16*).

The mean predictive accuracy factor (MPAF = mean(prediction/observation)) and the R^2 from a linear regression forced through 0 were determined to objectively compare model predictions with measured data. The MPAFs for carbamazepine and diclofenac are 1.0 and 1.1, respectively (excluding the clearly identifiable outlier). This shows that there is no bias in the model prediction. The R^2 values ($R^2_{carbamazepine} = 0.78$ and $R^2_{diclofenac} = 0.94$) indicate that consumption is proportional to population and that no significant elimination occurs with increasing flow distances in natural water bodies. This even holds true for diclofenac, which is prone to photodegradation. Comparing the results for diclofenac with and without elimination in lakes reveals no large difference. The population density downstream from lakes is higher than upstream, and after short distances, large WWTPs contribute substantially to the total pollutant load in these rivers. Only measurements directly at the outlet of lakes would deviate significantly because they are practically zero.

Besides carbamazepine and diclofenac 60 other substances (see list in SI 3) were evaluated against a reduced number of measurements. Similarly, good agreements between predicted and measured loads were achieved for widely applied substances including eight pharmaceuticals (two beta-blockers (atenolol and sotalol), four antibiotics (clarithromycin, sulfamethoxazole, sulfapyridine, trimethoprim), one anti-inflammatory drug (naproxen), and one anticonvulsant (primidone)), along with one insecticide (diazinon) and one anticorrosive (benzotriazole). Briefly, these compounds were detected in all WWTP effluents and river samples, except for naproxen, which was detected in all effluents but in only two river samples above the limit of detection. MPAFs are between 0.8 and 3.4 and outliers are detected only rarely (see SI 6 to 8 for more details). Many of the 40 remaining compounds are often measured below the limit of detection. Furthermore, their consumption may be highly variable over time and space. This particularly holds true for substances used in agriculture and material protection. Some may be transported predominantly during rain events, entering the watercourses through different pathways

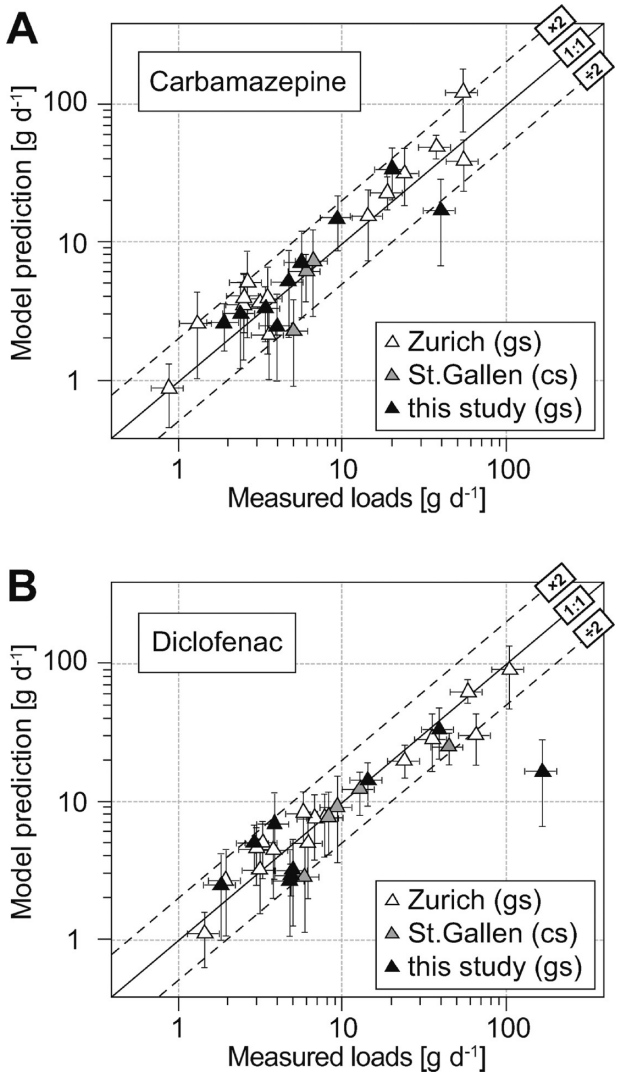

FIGURE 2. Model prediction vs measurements for daily carbamazepine and diclofenac loads in rivers (gs = grab sample, cs = composite sample). For measured values only the uncertainty due to chemical analyses is reflected with the uncertainty bars (±20%, *x*-axis). The two additional uncertain factors for predicted daily loads (±50% influent load and ±20% elimination rate variation) result in a total maximum uncertainty of ±64%, which is the 95%-quantile derived from the results of 10,000 Monte Carlo simulation runs (see text for more details).

(surface runoff). Therefore, they are not expected to directly correlate with the number of inhabitants in a catchment.

Outliers. For the outlier in Figure 2B, where almost ten times more diclofenac was measured than predicted, sampling and analytical errors can be excluded. Samples from the only upstream WWTP (120,000 actual PE, quite large for Swiss conditions) were collected the same day. Influent and effluent also showed ten times higher diclofenac loads than expected, still providing the typical WWTP removal rate. The few outliers deviating by more than a factor of 4 (see figures in SI 7 for the ten other substances) indicate that not all exposure scenarios can be captured with our model. However, even more complex water quality models accounting for degradation processes in a detailed mechanistic way (natural and WWTP) are unlikely to provide better results in such cases due to the lack of detailed, geo-referenced input information on industry, illegal discharge, or unknown high temporal variation of consumption in a particular catchment. Repeated measurements would have to be carried out to confirm high values and determine "natural" daily or seasonal variation (*21*). For validation purposes, both, a simple and a complex model require carefully collected samples, reliably analyzed concentrations, and proper flow data. Thus, obtaining representative measurements is often far more crucial and problematic than setting up the model itself.

Pollutant Concentrations. High concentrations due to low dilution are particularly encountered in the densely populated Swiss midland. Due to the good agreement between predicted and observed loads (Figure 2) PEC were calculated for base flow conditions ($Q_{95\%}$). The results are plotted in Figure 3A−D for carbamazepine and diclofenac in comparison to the predicted no effect concentrations (PNEC) taken from the WQC recommended by Jahnel et al. (*7*). When only the parent compound was considered, the PEC for carbamazepine are ubiquitously below the PNEC of 0.5 μg L^{-1} (Figure 3A). In contrast, the PEC for diclofenac exceed the PNEC of 0.1 μg L^{-1}, directly downstream from 125 WWTPs out of 543 sections with a known $Q_{95\%}$ (Figure 3B).

Metabolites have rarely been measured in environmental samples. As a first approximation, the ratio of metabolites to parent compound in WWTP effluents and rivers is assumed to be similar to the excreted fractions. In that case, the corresponding PNEC, considering the parent compounds and the toxicity equivalents from metabolites (values Table 1), are exceeded in 91 river sections for carbamazepine (Figure 3C) and in 224 river sections for diclofenac (Figure 3D). Coincidentally, the PNEC for diclofenac is exceeded in river sections with a dilution factor smaller than ten. Note that this dilution factor was derived based on pollutant loads cumulated along the rivers (cumulated wastewater), and does not relate to the local dilution factor used as default value in regulatory risk assessments (see SI 4).

Whether full elimination of diclofenac in lakes is accounted for or not does not lead to a significantly different prediction of diclofenac concentrations. If elimination in lakes is not considered, the PNEC for diclofenac including metabolites would be exceeded in 232 river sections instead of 224, a difference of only +3.5%.

Relevant Flow Conditions. Consideration of $Q_{95\%}$ for dilution represents a worst-case scenario, and hence the WQC may only be exceeded 5% of the time. To confirm or reject this hypothesis, 20 river sections were evaluated where long-term discharge information was available (not included in the model). Diclofenac loads were predicted with the model for these 20 locations assuming that diclofenac was consumed in the same amounts over the last 20 years. In an external routine we retrospectively analyzed at how many days per year the PNEC for diclofenac would have theoretically been exceeded (Figure 4A and B).

In Figure 4A a yearly analysis is shown for the river Ergolz up- and downstream from the WWTP Füllinsdorf. Downstream from the WWTP, the PNEC for diclofenac would have been exceeded on average 50% of the time, or 70% of the time when including metabolites. Just upstream from the WWTP the PNEC for diclofenac would have been exceeded 20% of the time, or 40% of the time when including metabolites, due to the 17 WWTPs located upstream. Year to year variation highly depends on the location (upstream or downstream of the WWTP) and if metabolites are considered or not. As presented in Figure 4B the analysis was repeated at 19 other locations, indicating the percentage of days per year during which the PEC for diclofenac exceeded the PNEC on average. Gauging stations are primarily located on larger rivers; typically these are locations with high dilution. Despite this unintentionally biased selection, the picture is consistent with Figure 3D. For river sections where an exceedance of the WQC is predicted at $Q_{95\%}$, this long-term analysis shows that it is, in most cases, more than a "5% of the time problem".

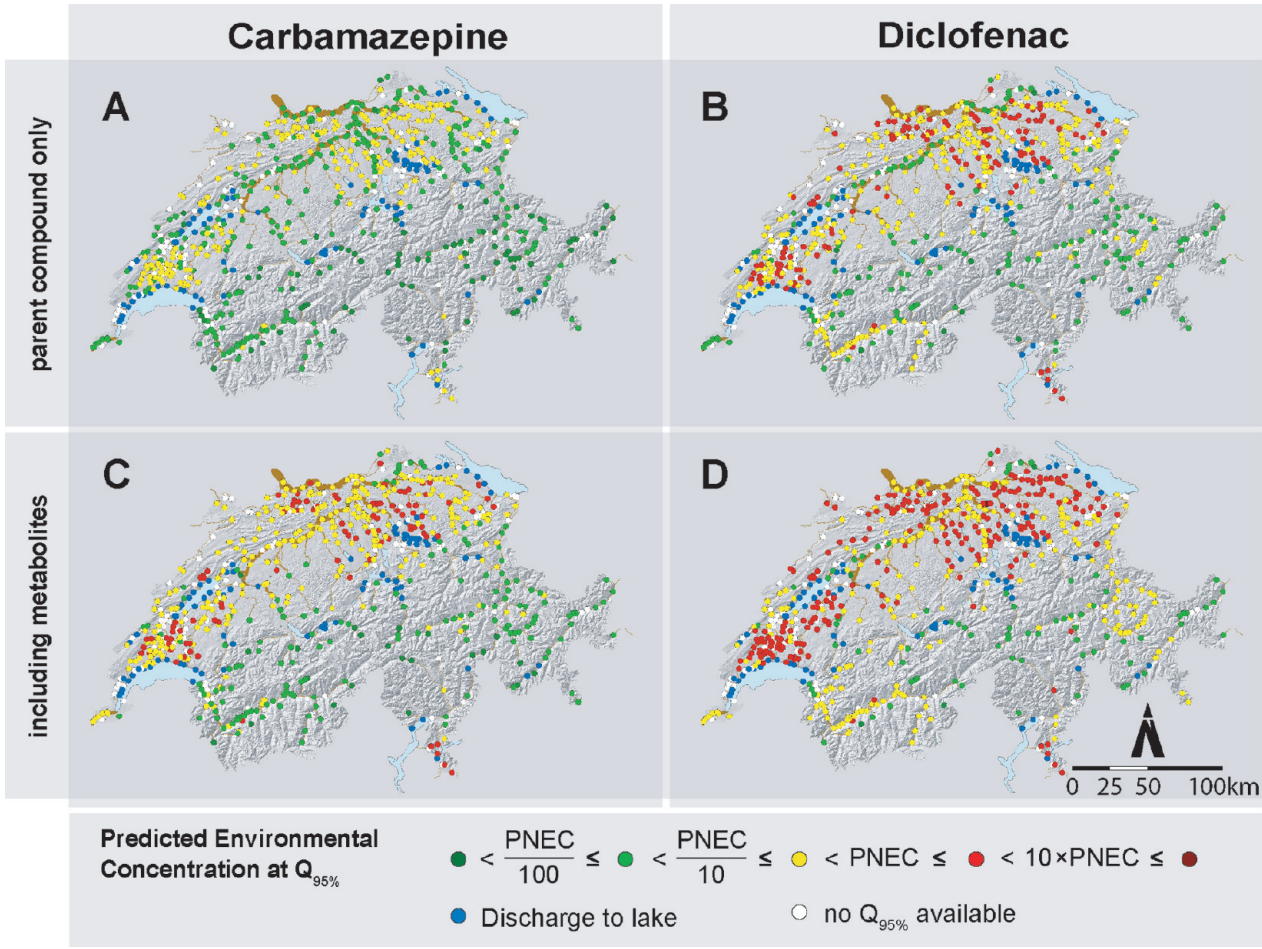

FIGURE 3. Predicted environmental concentrations (PEC) for carbamazepine and diclofenac at base flow conditions ($Q_{95\%}$). Panels A and B are the PEC only accounting for the excreted parent compound of carbamazepine and diclofenac, whereas panels C and D include their metabolites. Predicted no effect concentrations (PNEC) are taken from the water quality criteria recommended by Jahnel et al. (*7*): $PNEC_{carbamazepine} = 0.5\ \mu g\ L^{-1}$ and $PNEC_{diclofenac} = 0.1\ \mu g\ L^{-1}$. Red dots indicate river sections downstream from WWTPs in which the corresponding PNEC is exceeded. Maps reproduced by permission of swisstopo (BA081497).

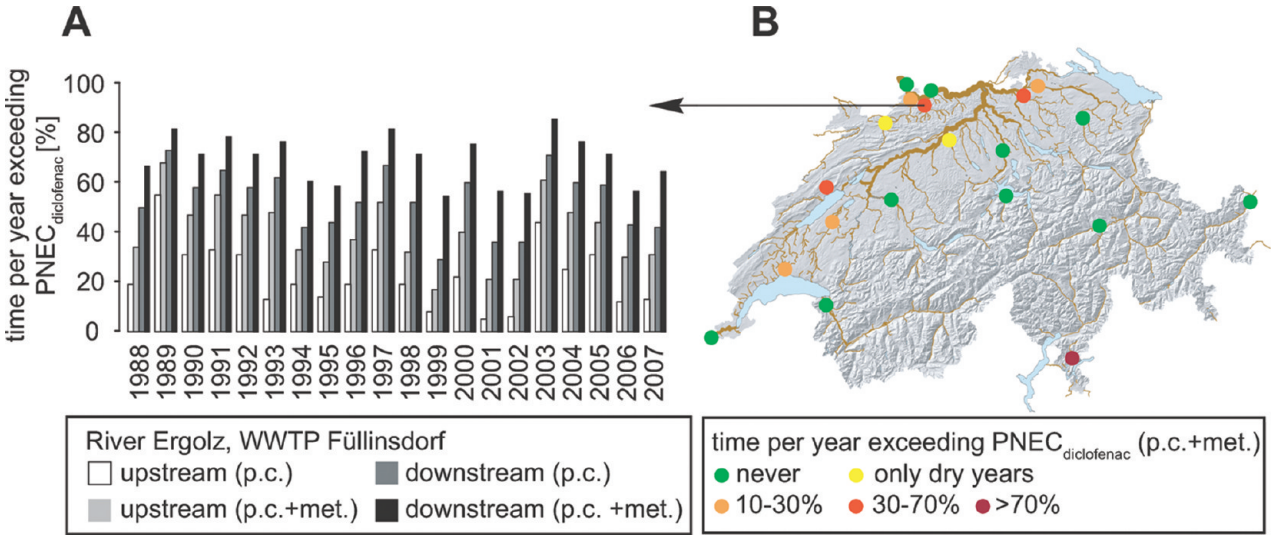

FIGURE 4. (A) Calculated percentage of days per year exceeding $PNEC_{diclofenac} = 0.1\ \mu g\ L^{-1}$ in the river Ergolz upstream and downstream of WWTP Füllinsdorf for parent compound only (p.c.) and for parent compound including metabolites (p.c. + met.). (B) Corresponding analysis for 20 river sections averaged over 20 years (diclofenac, p.c. + met.). Map reproduced by permission of swisstopo (BA081497).

Reduction Strategies. The results for the three strategies are summarized in Table 2. Following the "Water Quality" strategy, it is obvious that an upgrade of a WWTP also has a positive impact on the evaluation of WWTPs discharging to river sections farther downstream. To avoid exceeding 0.1 $\mu g\ L^{-1}$ diclofenac (including metabolites) downstream from 224 WWTPs (Figure 3D), a minimum of 173 WWTPs would have to be upgraded. As many of these are small to medium-

TABLE 2. Comparison of Strategies Given Different Goals for the Reduction of Micropollutants Discharged via WWTPs to Receiving Waters (The Evaluation Is Done for Diclofenac (DCF) Including Its Metabolites, with the Water Quality Criterion $PNEC_{DCF} = 0.1\ \mu g\ L^{-1}$ for River Sections Directly Downstream from 543 WWTPs with Known Base Flow $Q_{95\%}$)

	Water Quality ($C_{DCF} < 0.1\ \mu g\ L^{-1}$)	Load Reduction (WWTPs > 10,000 PE)	Combination (1. WWTPs > 100,000 PE; 2. $C_{DCF} < 0.1\ \mu g\ L^{-1}$)
no. of WWTP to be upgraded	173[a,b] [171, 110−206[b]][c]	197[a] [197][c]	181[a,b] [143, 120−218[b]][c,d]
resulting overall load reduction	∼30%[a] [27, 19−32%][c]	>80%[a] [>80%][c]	∼50%[a] [50%, 45−53%][c]
reduction of no. of river sections exceeding 0.1 μg L^{-1} DCF after upgrading	100%[a] [100%][c]	45%[a] [42%, 35−54%][c]	100%[a] [100%][c]

[a] Calculation with expected values. [b] If for all river sections downstream from WWTPs a $Q_{95\%}$ were available, this number might increase (for 117 of 660 no estimation is possible). [c] Values are obtained when the model takes uncertainty into account [median, 95%-quantiles], see text for more details. [d] This strategy results in a highly skewed distribution, therefore, results with expected values and the median do deviate more than in the two other strategies.

sized, this results in an overall load reduction of only 30%. To effectively protect drinking water resources and take responsibility for downstream riparian states, the "Load Reduction" strategy may be more appropriate. If the 197 WWTPs, each with more than 10,000 PE, were upgraded an overall load reduction of more than 80% would result. However, water quality is compromised, and only 45% of the river sections would be prevented from exceeding 0.1 μg L^{-1} diclofenac. The "Combination" strategy initially upgraded 12 WWTPs, each with more than 100,000 PE, achieving already 30% load reduction and then the "Water Quality" strategy was applied. This combined strategy requires that a total of 181 WWTPs be upgraded, resulting in a total load reduction of 50%, and no exceedance of the WQC. Irrespective of which strategy will be followed to reduce diclofenac loads and concentrations, it would be a considerable number of WWTPs, implying a substantial investment.

Effect of Uncertainty and Implication for Decision Making. The uncertainty bars in Figure 2 (y-axis) reflect the 95%-quantiles for predicted daily loads obtained from 10,000 Monte Carlo simulation runs. While a maximum of ±64% was identified for river sections receiving wastewater from only one WWTP, the uncertainty decreases for river sections farther downstream with the increasing number of WWTP discharges: a higher load from a WWTP upstream can be compensated by a lower load from a WWTP downstream, narrowing the 95%-quantile.

Additionally considering the uncertainty of dilution, the Monte Carlo simulation leads to between 110 and 218 river sections exceeding 0.1 μg diclofenac L^{-1} including metabolites (95%-quantile, see Table 2). This is approximately plus 20% and minus 40% when compared to the results calculated with expected values (224 river sections). Whenever the "Water Quality" strategy is involved, this relative uncertainty range is also being reflected in the number of WWTPs requiring upgrades. This refers to the cost side of a cost−benefit analysis. For a fixed selection of WWTPs to be upgraded, i.e. the "Load Reduction" strategy, "no uncertainty" is associated with the number of WWTPs and hence costs. Uncertainty is instead reflected in the benefit, if benefit is measured with water quality, i.e., the number of river sections no longer exceeding the WQC rather than load reduction.

In view of the results (including prediction uncertainty) our model proves to be a very valuable decision support tool. It substantiates the requirement for evaluating water quality criteria across broader catchments rather than based on single river sections which may be well studied but are not representative. Given the consumed amounts of the twelve compounds investigated in this study and their current corresponding recommendations for water quality criteria, diclofenac demands for the largest need for action. Advanced treatment technologies would of course also reduce the discharge of many other substances, not only the closely investigated pharmaceuticals diclofenac or carbamazepine. This is beneficial since the knowledge of the ecological impact of mixture effects is, to a large extent, lacking. Additionally, ozonation for example also provides disinfection and reduces color and odor.

Outlook. The application of water quality criteria must be clearly defined: should they apply to mean concentrations, concentrations at mean annual flow, or even base flow conditions ($Q_{95\%}$)? Such choices will influence decisively the need for action and investment. However, the model already answers many "what if" questions arising in cost−benefit analyses and the long-term planning process of prospective environmental protection agencies and WWTP operators. Once the water quality criteria are determined, the model will be further applied for setting up sensitive monitoring campaigns, including chemical analyses and bioassays, at identified hotspots. These shall confirm the successful reduction of micropollutant loads, and inherent enhanced water quality.

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Supporting Information Available

Further information referred to in the main text of this paper is available as a PDF: an example for graph theory, details on sampling and chemical analysis, list of all compounds analyzed for, assessment of dilution factors at base flow ($Q_{95\%}$) and of uncertainty related to $Q_{95\%}$ values, sampling procedure for Monte Carlo simulation to assess prediction uncertainty, model input data for ten additional compounds, model results for these compounds, and an evaluation of results. An Excel spreadsheet provides raw data from the study. This information is available free of charge via the Internet at http://pubs.acs.org.

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