



European-wide spatial analysis of sewage treatment plants and the possible benefits to nature of advanced treatment to reduce pharmaceutical emissions

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ABSTRACT

Pharmaceuticals are known to widely occur in the environment and to affect the health of ecosystems. Sewage treatment plants (STPs) are main emission pathways for pharmaceuticals, which are often not sufficiently removed during wastewater treatment. In Europe, STP treatment requirements are specified under the Urban WasteWater Treatment Directive (UWWTD). The introduction of advanced treatment techniques, such as ozonation and activated carbon, under the UWWTD is expected to be an important option to reduce pharmaceutical emissions. In this study, we present a European-wide analysis of STPs reported under the UWWTD, their current treatment level and potential to remove a set of 58 prioritised pharmaceuticals. Three different scenarios were analysed to show 1) UWWTD present effectiveness, 2) the effectiveness at full UWWTD compliance, and 3) the effectiveness when advanced treatment is implemented at STPs with a treatment capacity of >100.000 person equivalents. Based on a literature study, the potential of individual STPs to reduce pharmaceutical emissions ranged from an average of 9% for STPs with primary treatment to 84% for STPs applying advanced treatment. Results of our calculations show that European-wide emission of pharmaceuticals can be reduced with 68% when large STPs are updated with advanced treatment, but spatial differences exist. We argue that adequate attention should also be paid with regards to preventing environmental impacts of STPs with a capacity <100.000 p.e. Circa 44% of total STP effluent is emitted near Natura2000 sites (EU nature protection areas). Of all surface waters receiving STP effluent for which the ecological status has been assessed under the Water Framework Directive, 77% have a status of less than good. Relatively often only primary treatment is applied to wastewater emitted into coastal waters. This analysis can be used to further model pharmaceutical concentrations in European surface waters, to identify STPs for which more advanced treatment might be required and to protect EU aquatic biodiversity.

1. Introduction

Pharmaceuticals help to increase the longevity and quality of life for many people. However, the widespread use of human and veterinary pharmaceuticals also results in releases to the aquatic environment (Auser Beek et al., 2016). This is of concern as most pharmaceuticals are designed to be highly active at low concentrations and resistant to biodegradation (Khetan and Collins, 2007). Active pharmaceutical ingredients and their transformation products have widely been detected in surface water, groundwater and drinking water (Houtman et al., 2014; Schulze et al., 2019; Zhou et al., 2019). At some locations

pharmaceuticals are already present at levels deemed unsafe, classifying them as a global threat to both human and environmental health (Wilkinson et al., 2022). The global consumption of pharmaceuticals has increased over the last decades (Klein et al., 2018) and is expected to rise further due to multiple factors, including changes and innovations in clinical practices, ageing populations and higher market availability, potentially amplifying already existing environmental concentrations (Belloni et al., 2016; Bernhardt et al., 2017; Bunke et al., 2019; Nagesh et al., 2022; OECD, 2021).

Pharmaceuticals may be emitted as a result from production, patient excretion and incorrect disposal (Straub, 2016). In order to protect

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water sources from pharmaceutical pollution, multiple actions can be taken over the whole chemical life-cycle (OECD, 2019; Wezel et al., 2017). Options early in the chemical life-cycle, include the design of Safe and Sustainable substances and personalised healthcare, are often preferred as they are more cost-effective (Puhlmann et al., 2021). Via patient excrements, pharmaceuticals and their metabolites can enter the wastewater systems where they are not sufficiently removed and are consequently released into the environment (Luo et al., 2014). End-of-pipe measures such as the treatment of wastewater will remain indispensable, as it is clear that pharmaceuticals will continue to be needed and will thus continue to be released into the wastewater (Kümmerer et al., 2018). Sewage treatment plants (STPs) are of special relevance as households are seen as one of the most important emission sources of pharmaceuticals to wastewater (Adeleye et al., 2022; Comber et al., 2015; Michael et al., 2013), except for specific types of pharmaceuticals which are mainly emitted via hospitals and health institutions (Herrmann et al., 2015; Le Corre et al., 2012).

In the EU, the Water Framework Directive (WFD) is implemented to protect surface waters, transitional waters, coastal waters and groundwater (Directive 2000/60/EC). A key aim of the WFD is to achieve a 'good ecological status' for all water bodies, which is influenced amongst others by water quality. Measurements according to the WFD regularly take place within Natura2000 sites; a network of key breeding and resting sites for rare and threatened species, and some rare natural habitat types that the WFD (Annex V No. 1.3.5) specifically refers to. A good ecological condition of aquatic systems is important to ensure delivery of ecosystem services in the future (Grizzetti et al., 2019), and an important aim of the EU Biodiversity Strategy (European Commission, 2020a). According to the latest assessment, however, a good ecological status has only been achieved for 40% of European surface waters, and chemicals released via STPs are identified as one of the main pressures on these surface water bodies (EEA, 2018a; Lemm et al., 2021).

The WFD also links to the EU Urban Wastewater Treatment Directive (UWWTD, 91/271/EEC). The objective of this Directive is to protect the environment for adverse effects of urban waste water, and concerns its collection, treatment and discharge. The UWWTD sets maximum concentrations for the nitrogen, phosphorous and organic matter content for treated wastewater, but does not address micropollutants such as pharmaceuticals yet. The WFD does include several pharmaceutical substances on the so-called 'Watch List' (European Commission, 2022a). In the proposal for a revised UWWTD, the European Commission lays down the aim to implement advanced treatment to STPs treating a load equal to or greater than 100,000 person equivalents (p.e.) by 31 December 2035 at the latest (European Commission, 2022b). As also mentioned in the Strategic Approach to Pharmaceuticals in the Environment, the European Commission will investigate the feasibility of upgrading selected STPs to more advanced treatment technologies (European Commission, 2020b).

A wide range of advanced treatment methods have been investigated for the removal of pharmaceuticals from wastewater, for which either ozonation or activated carbon treatment are reported to be the best performing and most cost-effective (Kosek et al., 2020; Logar et al., 2014; Rout et al., 2021). Advanced treatment techniques have already been implemented in Switzerland at selected STPs as part of the Swiss water conservation legislation introduced in 2016 (Stamm et al., 2015). By following this approach, the pressure of pollution on Swiss surface waters is estimated to be reduced by 50% (FOEN, 2015). A recent study by Pistocchi et al. (2022a) estimates that by following a similar approach in the entire EU, the cumulative toxicity of STP effluent will be reduced by circa 36%. Certain knowledge gaps however still remain. For example, removal rates as used in the Pistocchi et al. (2022a) study were mainly assumed using models. This results in high uncertainties as it is still difficult to generically model the fate of chemicals in advanced treatment processes due to the influence of, amongst others, specific process conditions influence removal efficiencies (Fischer et al., 2019).

Inclusion of experimental data might provide better insights in the removal of chemicals in STPs and reduce uncertainties (Pistocchi et al., 2022a).

In this study, experimental removal rates are derived from an extensive literature research. Next, we aim to assess the effectiveness of European STPs to reduce pharmaceutical emissions for a 1) Present, 2) Full Compliance and 3) Advanced Treatment scenario. In addition, spatial variation between European STPs are assessed for all European river basins taking into account their ecological status as assessed under the WFD, as well as proximity to Natura 2000 sites. For the Advanced Treatment scenario, we follow the approach by Pistocchi et al. (2022a) in order to show the present effectiveness and the possible value of introducing advanced treatment at large STPs (>100 000 p.e.).

2. Methods

2.1. Waste water treatment scenarios

Three different scenarios were analysed in this study. For every STP in the EU, we considered 1) the present level of treatment (Present scenario), 2) full compliance with the UWWTD in its current form (Full Compliance scenario) and 3) a scenario where more advanced treatment, either with ozonation or activated carbon, is required at large STPs (Advanced Treatment scenario). For the Full Compliance scenario, envisioned changes to non-compliant STPs as reported under article 17 of the UWWTD were used to calculate the total capacity (in p.e.) per treatment level (EEA, 2022a). For the Full Compliance and the Advanced Treatment scenarios, it was also assumed that 100% of the population is connected to a STP. In addition, for the Advanced Treatment scenario, all STPs with a capacity of $\geq 100,000$ p.e. were assigned with advanced treatment (ozonation or activated carbon).

In Fig. 1 a workflow is presented to calculate the population (in p.e.) per treatment level. First, data collected under Article 15 of the UWWTD for the year 2020 and reported in Waterbase v8 (EEA, 2022a) was used to assign treatment levels to individual STPs for the present scenario. Waterbase contains information on the location and characteristics of urban STPs with generated wastewater loads above 2 000 population equivalents (p.e.) for all EU member states. Based on availability of data, 23,568 STPs were selected for our assessment. See S11 for more detailed description on steps taken to filter the data. Treatment levels were defined following UWWTD and OECD definitions (OECD, 2003) as primary, secondary, tertiary, disinfection or advanced treatment (ozonation or activated carbon). Next, the total capacity (in p.e.) per treatment level was calculated for 5 regions in Europe (see Table 1), defined according to divisions used in the EEA indicator assessment (EEA, 2017). Data on the total STP capacity per treatment level was combined with Eurostat data on the percentage of residents that is not connected to STPs (Eurostat, 2022). At time of the analysis, Eurostat contained data till 2019. Hence, for most countries data for the year 2019 was used or the latest data available in the database. Details on the percentage of residents per member state that are not connected an STP are shown in S11 (Table S1.1).

2.2. Selected pharmaceuticals and their STP removal rates

A list of 58 pharmaceuticals posing the highest risk to aquatic systems was compiled based on already existing prioritisation lists, including both parent compounds and metabolites (de Voogt et al., 2009; European Commission, 2020c; FOEN, 2015; NORMAN Network, 2014; Zhou et al., 2019). Removal efficiencies of these substances by different wastewater treatment techniques were collected in the scientific literature. According to the approach first introduced in Switzerland, upgraded STPs will contain either ozonation or activated carbon treatment. The removal rates of STPs that apply ozonation or activated carbon were combined in this study and averaged to obtain the removal rate for advanced treatment. Based on the identified references

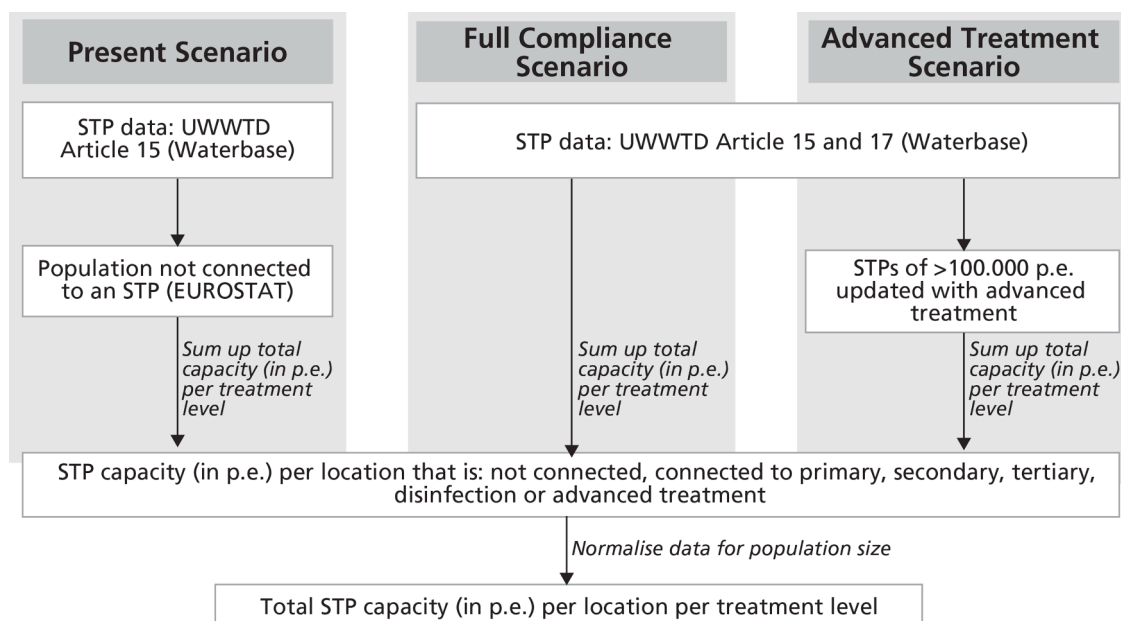


Fig. 1. Workflow for calculating the total population per European region that is connected to a certain treatment level under the Present, Full Compliance and Advanced Treatment Scenarios.

Table 1

Overview of the different European regions defined in this study.

Region	Countries	Total population (in 2020 or 2019)
North	Norway, Sweden, Finland	16.387.131
Central	Austria, Belgium, Denmark, Germany, Ireland, Luxembourg, the Netherlands, the United Kingdom	200.242.146
South	Cyprus, Greece, France, Italy, Malta, Spain, Portugal	197.187.604
East	Czechia, Estonia, Hungary, Latvia, Lithuania, Poland, Slovenia, Slovakia	71.990.553
South-East	Bulgaria, Croatia, Romania	30.286.952

(63 in total), removal rates were calculated per pharmaceutical per STP with a specific treatment type. Only total removal rates were used from full scale STPs which apply a combination of techniques. Next, the average removal rate over all substances was used to estimate the fraction being released to the environment and being removed per treatment level. A more extensive description of the literature search and calculation method is given in the SI1.

2.3. Spatial analysis

The location of STPs and their proximity to Natura2000 sites was assessed by using a buffer of 2.000 metre as in line with an earlier defined non-binding buffer zone (EEA, 2018b). Natura2000 sites were available for all countries except Norway and the United Kingdom (EEA, 2022b).

STP data was also combined with data on the ecological status (or potential) of water bodies in order to assess the total STP effluent (in p. e.) emitted into water bodies with a good or less than good ecological status. The ecological status of water bodies as defined under the 2nd River Basin Management Plans was derived from the WISE Water Framework Directive Database (EEA, 2021). Out of the 23.568 STPs reported under the UWWTD, information on the ecological status of water bodies into which effluent is emitted was available for 15.950 STPs. A more detailed description on how the datasets were combined is provided in SI1. All data analysis was performed in R and QGIS.

3. Results and discussion

3.1. Removal rates of pharmaceuticals in STPs

The removal rates of the 58 pharmaceuticals taken into account in this study for different STP treatment levels are shown in Fig. 2. For a couple of substances (e.g. acetaminophen, atenolol, carbamazepine, diclofenac, ibuprofen and sulfamethoxazole) relatively many data were available, whereas for other substances only few studies or no data could be found. Details on removal rates for individual substances can be found in the online data repository (van Dijk et al., 2023). Specifically for primary and tertiary treatment, up to 50% of individual pharmaceutical the literature search did not yield removal rates (black cells in Fig. 2). This can impact the validity and reliability of our analysis and potentially bias the calculated average STP removal rates. The calculated removal rates are furthermore biased by the compounds selected in this study. In the future, data gaps might be partly filled by using modelling approaches such as SimpleTreat (Struijs, 2014). However, SimpleTreat can only be used to calculate removal for primary and secondary treatment. Data gaps from the literature were partly found due to incomplete reporting of measured data on STP substance removal in the studies. Future studies would benefit from more transparent and accessible data on STP removal efficiencies (Fischer et al., 2019). It's important to acknowledge that our assessment may not cover all relevant pharmaceuticals, as pollution can vary by location and time, and there are a multitude of factors that can influence which pharmaceuticals are present in wastewater (Bunke et al., 2019; Massei et al., 2018; van Gils et al., 2019). Furthermore, it should be noted that this study focused solely on pharmaceuticals, and did not consider other types of substances such as biocides and chemicals registered under REACH. These substances can however also be important sources of pollution in surface waters (Posthuma et al., 2018; van Gils et al., 2020). When averaging the collected removal rates of all 58 pharmaceuticals per treatment and excluding data gaps, primary treatment has a removal potential of circa 9% (± 11), secondary treatment of 42% (± 27), tertiary treatment of 42% (± 27), disinfection of 66% (± 29) and advanced treatment of 84% (± 20) (Table 2). Average removal rates of advanced treatment lie above the removal criteria of $\geq 80\%$ earlier laid down in Switzerland (FOEN, 2015). Based on our analysis, six substances (Cyclophosphamide, Fluconazole, Gabapentin, Irbesartan, Oxypurinol,

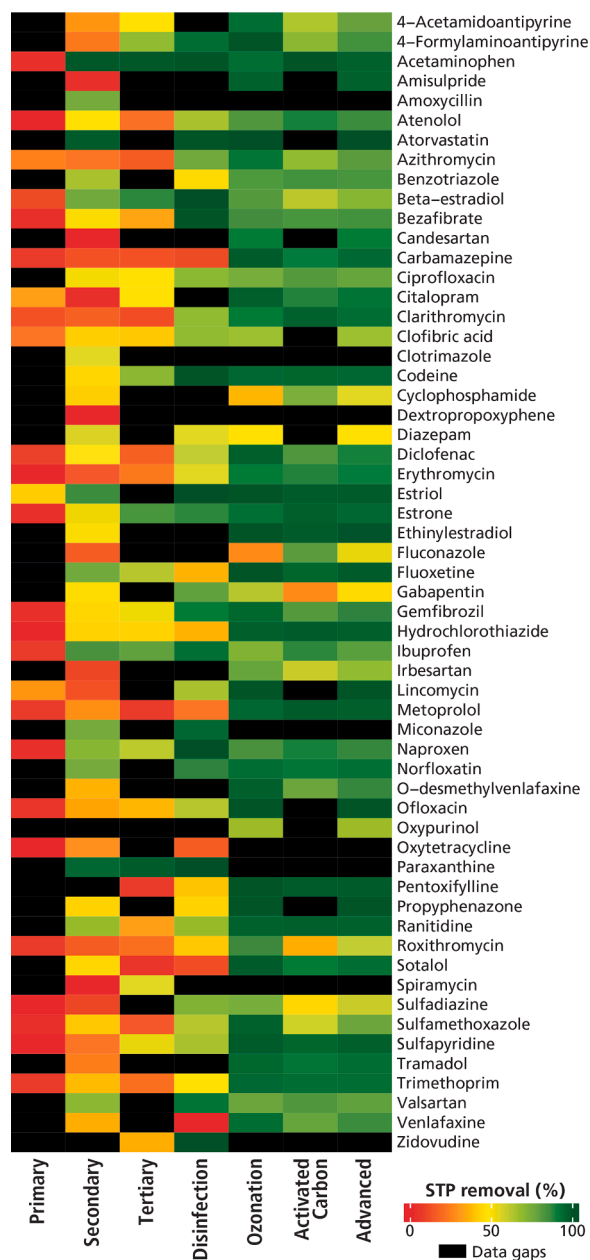


Fig. 2. Heatmap of the 58 pharmaceuticals and their removal rates in STPs by different treatment techniques. Removal rates refer to the removal by individual treatment levels. Data gaps are shown in black. Full calculations and references on the removal rates are reported in the open data repository (Dijk et al., 2023).

Table 2

Descriptive statistical parameters for STPs applying Primary, Secondary, Tertiary, Disinfection, Ozonation, Activated Carbon and Advanced treatments. Advanced treatment was calculated as the average from ozonation and activated carbon.

Treatment Level	Number of substances with data (out of 58)	Average removal (%)	Stdv (%)	Min. removal (%)	Max removal (%)	Median removal (%)
Primary	26	9	11	0	41	5
Secondary	55	42	27	0	99	42
Tertiary	33	42	27	5	99	40
Disinfection	43	66	29	0	100	68
Ozonation	50	87	16	27	100	93
Activated carbon	41	81	18	27	99	88
Advanced	50	84	20	27	100	89

Sulfadiazine) are however expected to not be well removed by ozonation or activated carbon treatment (Fig. 2). No significant difference (p value of 0.05) between ozonation and active carbon treatment was found (SI1). Furthermore, no significant difference between removal efficiencies of secondary and tertiary treatment was found, as well as between tertiary and disinfection treatment (SI, Table SI1.5). These findings can help to generate a better picture of pharmaceutical emissions to water bodies as most modelling exercises to date (e.g. in Oldenkamp et al., 2018; van Gils et al., 2020) rely on STP models such SimpleTreat and therefore only consider the fate and removal during primary and secondary treatment (Lautz et al., 2017; Struijs, 2014).

3.2. Removal rates and substance characteristics

Primary treatment intends to reduce the solid content of the wastewater (oils and fats, grease, sand, grit and settleable solids). Based on our search only 9% of the total pharmaceutical load can potentially be removed, which is in line with earlier reported total removal rates (Greenham et al., 2019). Substance removal by secondary treatment mainly depends on the sorption on the sewage sludge and their degradation or transformation during the treatment, and therefore likely removes the more hydrophobic and degradable pharmaceuticals (Michael et al., 2013). With regards to advanced treatment -ozonation or activated carbon- overall removal efficiencies are found to be similar in this study however differences might exist for the removal of some specific compounds. Treatment with activated carbon can for example be used for removing many hydrophobic and also some charged pharmaceuticals from water, whilst high removal after ozonation is usually observed for pharmaceuticals with one or more functional groups such as non-aromatic carbon-carbon double bonds, amines and activated aromatic rings and moieties (Ikehata et al., 2006; Michael et al., 2013). Polar chemicals are usually less well removed in STPs (Fischer et al., 2019; Gollong et al., 2022; Sjerps et al., 2021). Moreover, removal rates for non-aromatic compounds by activated carbon is often low, whilst compounds with unoxidable bonds are able to survive ozonation treatments (Hale et al., 2022). Additionally, ozonation can lead to the formation of undesired and highly reactive by-products. Hence, while ozonation and activated carbon can be effective in removing certain contaminants, they are not universally applicable. Following the approach reported by Pronk et al. (2020), who proposed a framework to estimate removal efficiencies of water treatment techniques based on substance characteristics, we could not identify a clear trend between substance properties and removal rates. This might be caused by different study designs or differences in the actual STP removal efficiency due to variations in i) quality of waste water entering the STPs, ii) operating conditions such as sludge retention time, hydraulic retention time and flow rate, and iii) other factors such as difference in climate (McLachlan et al., 2022; Michael et al., 2013; Pomiès et al., 2013; Yang et al., 2017).

3.3. Total STP removal potential

The Sankey diagrams of Fig. 3a-c show to what type of STP treatment level the population is connected and how the fraction of

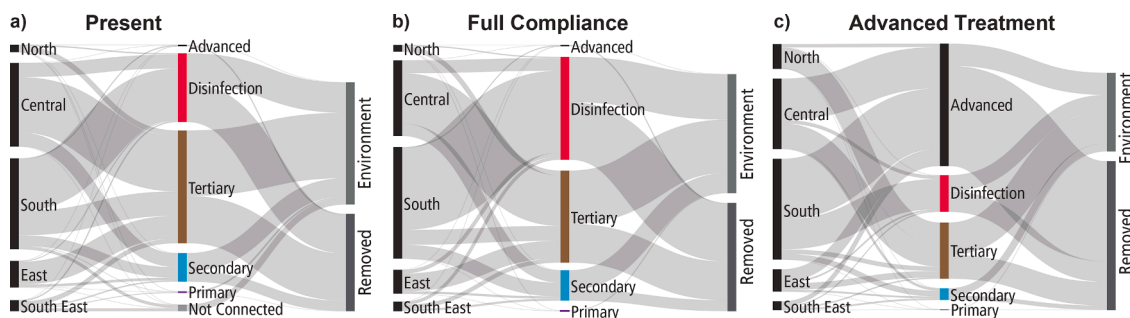


Fig. 3. The share of the European population connected to each type of STP treatment level and the percentage of pharmaceuticals that are either removed ('removed') or emitted ('environment') via STPs for each European region. Panel A represents the 'Present' scenario, Panel B the 'Full Compliance' scenario, and Panel C the 'Advanced Treatment' scenario, with a respective pharmaceutical emission reduction potential of 48% (± 27), 52% (± 28) and 69% (± 22).

pharmaceuticals is removed or emitted to the environment. At present, the potential to reduce environmental emissions of pharmaceuticals of all European STPs combined is 48% (± 27) (Fig. 3a). South-East Europe has currently the highest percentage of untreated wastewater. Around 25% of urban wastewater in this region is emitted without any treatment into freshwater systems. Other differences in treatment level can be observed for specific countries (Fig. 4). For example, in Southern Europe disinfection is applied relatively often even though this is not required under the UWWTD. This is likely the effect of national legislations. In Italy, for example, a disinfection step needs to be implemented at STPs with a capacity of 2000 p.e. or higher (Collivignarelli et al., 2017).

When full compliance would be reached with the current UWWTD, the STP removal potential is slightly increased to 52% (± 28) (Fig. 3b). Most changes in the Full Compliance scenario are observed in South, East and South-East Europe (Fig. 5) as -despite improvements over the last few years- these regions currently remain least compliant with the UWWTD (European Commission, 2022c). The fact that the current UWWTD has no focus on micropollutants such as pharmaceuticals is reflected by the relatively small increase of the STP potential to reduce pharmaceutical emissions in this Full Compliance scenario. Full compliance to the UWWTD is expected to mainly reduce the nutrient and microorganism loads of wastewater. In the Advanced Treatment scenario, the emission reduction potential for the selected pharmaceuticals is increased to 69% (± 22) (Fig. 3c). Advanced treatment is placed in bigger cities, and therefore most changes in this scenario are observed in more densely populated areas (Fig. 6).

In this study only STPs reported under the UWWTD were taken into account, meaning STPs with a capacity of $<2\,000$ p.e. are not included. 364 650 agglomerations with a capacity of 2000 p.e. or less -corresponding to circa 75 million inhabitants- have been identified and are predicted to impact receiving water bodies. The percentage of small agglomerations was on average higher in Czechia, Slovakia, Croatia, Slovenia, Romania and Poland (Pistocchi et al., 2022b). Future updates to the UWWTD will likely include smaller STPs in the UWWTD dataset (European Commission, 2022d), resulting in a complete picture of European STPs and their potential to reduce environmental emission of pharmaceuticals.

3.4. Spatial analysis

3.4.1. Water body types

For present day conditions relatively often only primary treatment is applied to STPs emitting into coastal waters as compared to STPs that emit into estuaries or fresh water bodies (Fig. 7). This can also be seen in Fig. 4, in which the geographical location of all STP and their treatment level under present day conditions are shown. Main reason for this is that the UWWTD does not specifically protect marine waters and many STPs are exempted from stricter treatment when primary treatment is in place (Article 2 (7) UWWTD). This is not in line with the WFD, which does specifically cover marine systems. The treatment level of

STPs emitting into coastal waters improves under the Advanced Treatment scenario at more densely populated areas. However, in other coastal areas from e.g. Norway and Croatia mainly primary treatment is applied under all scenarios (Fig. 4 and Figure S11.1). This is reason of concern as pharmaceutical pollution already affects marine ecosystems (Fabbri and Franzellitti, 2016; Mezzelani et al., 2018). Under the Advanced Treatment scenario, treatment level is improved for STPs emitting into all water types. STP effluent emitted into lakes also receive relatively lower treatment compared to rivers and transitional waters. Different water body types may respond different to (chemical) stressors (Birk et al., 2020; Reid et al., 2019). STPs emitting into smaller water bodies (Figure S11.2) might be prioritised as, for example, large rivers are reported to be less impacted by chemical pollution due to their higher dilution capacity compared to other river types (Lemm et al., 2021). Future modelling studies should furthermore take chemical consumption data into account to assess whether water bodies and their ecosystems are sufficiently protected and to make (cost-)effective decisions in water quality management with regards to implementation of advanced treatment techniques (Coppens et al., 2015).

3.4.2. Ecological status under the WFD

At present, 15,950 out of the 23,568 STPs (with a total treatment capacity of $5.4e+8$ p.e.) emit treated effluent into a surface water bodies for which information on the ecological status was available. From Fig. 8 it can be observed that most (12,396 STPs; with a total treatment capacity of $4.5e+8$ p.e.) of these 15,950 STPs emit treated wastewater into water bodies which have a less than good ecological status, while water bodies with a good or high ecological status are influenced by less than $1e+8$ p.e. Few changes are observed with regards to STP treatment levels under the Full Compliance scenario compared to the Present scenario (Figures S11.6 and S11.7). The Full Compliance scenario, based on envisioned changes reported under Article 17 of the UWWTD, primarily involves improving the performance of existing underperforming STPs through maintenance or expansion. It is anticipated that such changes will mainly lead to a reduction in nutrient enrichment of surface waters, which is one of the main pressures hampering a good ecological status of water bodies together with chemical pollution and habitat alterations (EEA, 2018a). In the Advanced Treatment scenario 809 (total treatment capacity of $2.8e+8$ p.e.) out of the 15,950 STPs are updated with advanced treatment (Fig. 8), which has the potential to reduce the pressure of chemical pollution and improve their ecological status.

Management of water at the river basin level is key for implementing the WFD. Under all scenarios, only primary or secondary treatment techniques are applied to most of the generated wastewater load in some RBDs in Croatia, France, Norway, Poland, Portugal and the UK (Figure S11.5), whereas some waterbodies in these RBDs have a less than good ecological status (EEA, 2021). Next to prioritization based on a p.e. cut-off, it may be beneficial to prioritise STPs for advanced treatment based on the ecological status. All relevant pressures need to be considered in order to make decisions on the implementation of

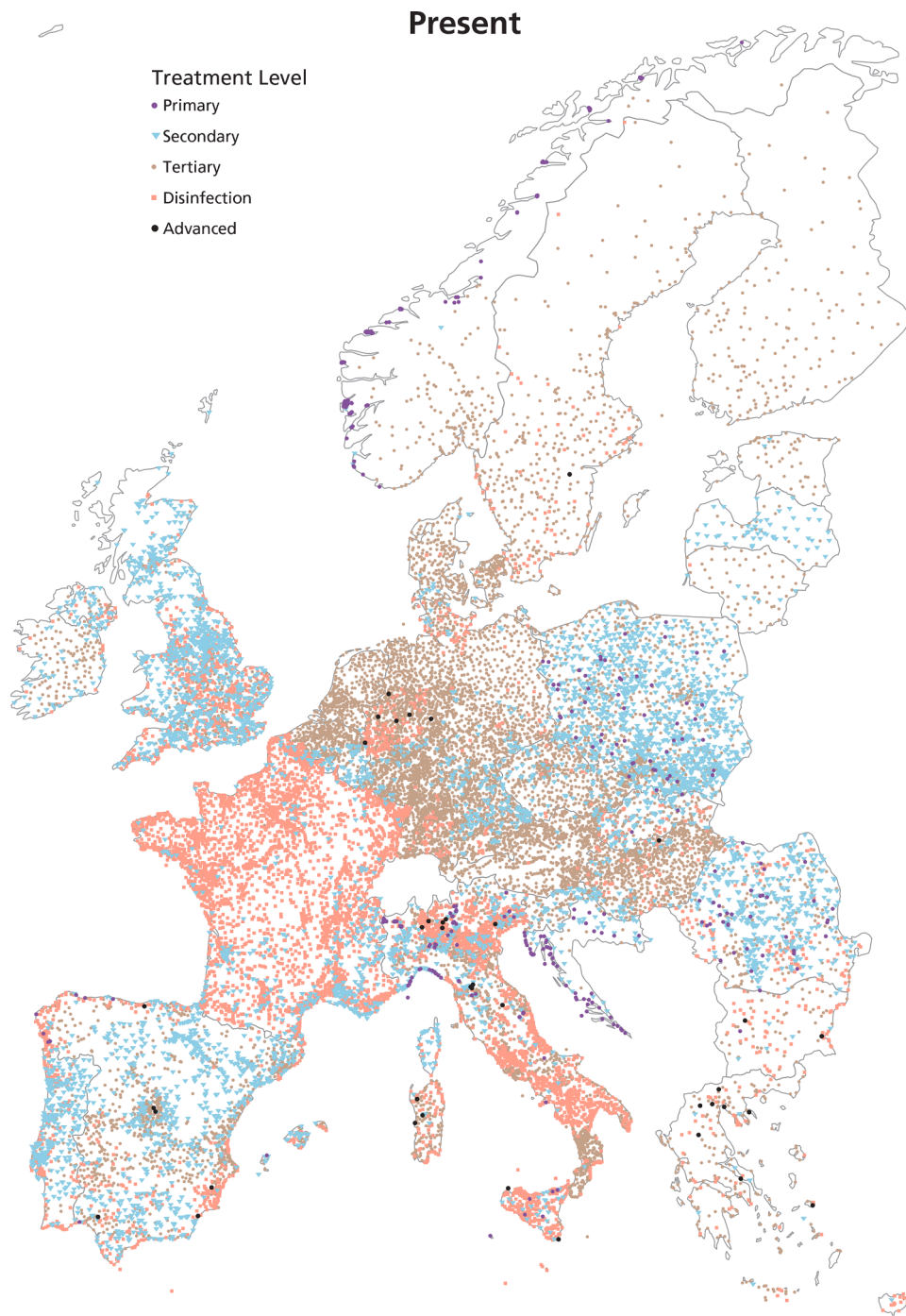


Fig. 4. STPs and their treatment level under the Present Scenario.

advanced techniques or other measures to help restore and protect freshwater ecosystems (Carvalho et al., 2019; Lemm et al., 2021, 2019).

3.4.3. Natura2000 sites

At present, circa 44% of all treated effluent (corresponding to 3.1×10^8 p.e.) is emitted directly within Natura2000 sites or the 2 km buffer zone (Fig. 9). Most of the effluent undergoes tertiary treatment. When envisioned changes reported under article 17 of the UWWTD are made under the Full Compliance scenario, some STPs are no longer used and new STPs are constructed. Outside Natura2000 sites this will result in an increase of total treated effluent, and an increase in the amount of effluent treated with a disinfection step. For STPs emitting in or close to Natura2000 however relatively few changes are observed. Under the

Advanced Treatment scenario, 38% of all effluent will be treated with advanced treatment. Then, no difference in treatment level can be observed between STPs located near and further away from Natura2000 areas in any of the scenarios. As STPs are identified as one of the main stressors affecting ecological status (EEA, 2018a; Lemm et al., 2021), STPs emitting effluent emitted near Natura2000 sites could be prioritised for implementation of advanced treatment as well. This might especially be relevant in Central Europe, as here the smallest share of effluent is treated with advanced treatment steps (Figure SI1.3).

3.5. Benefits and considerations of advanced treatment

Given that not all substances are sufficiently removed by advanced

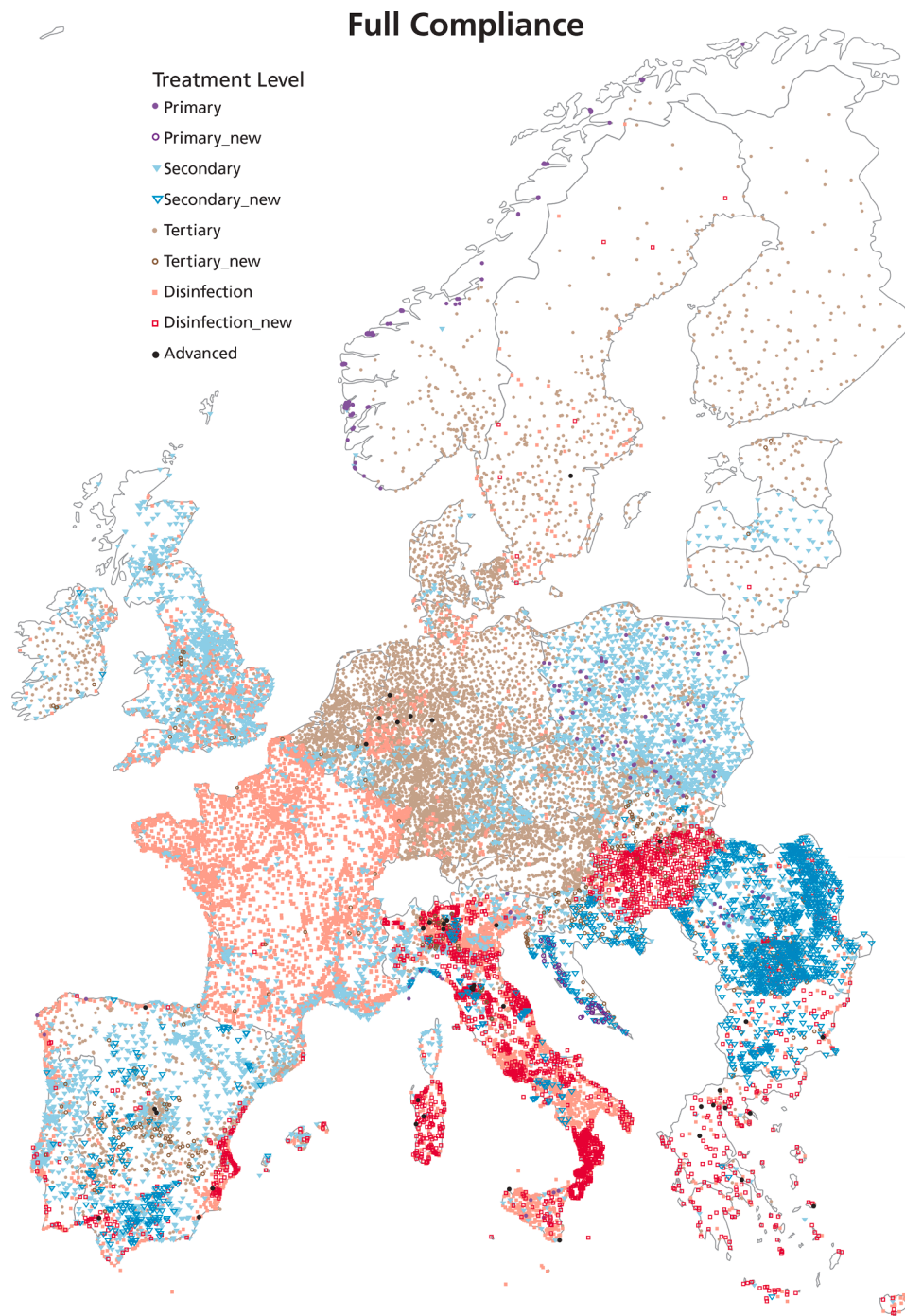


Fig. 5. STPs and their treatment level under the Full Compliance Scenario. New or upgraded STPs are shown in the figure as Primary_new, Secondary_new, Tertiary_new and Disinfection_new.

treatment techniques and that it is not feasible to update all STPs (Piscocchi et al., 2022c), other measures focussing on input prevention need to be considered as well (Kümmerer et al., 2019; Wezel et al., 2017). Furthermore, the increased use of chemicals (Bunke et al., 2019; Nagesh et al., 2022) and demand for clean water (Boretti and Rosa, 2019) asks for a paradigm shift in wastewater management where adequately treated wastewater can for example be re-used (Dingemans et al., 2020; Villarín and Merel, 2020). Climate change is projected to further reduce water availability in sufficient quantity and quality, emphasising the importance of such water reuse practices.

The current study may be used to further model pharmaceutical concentrations in European surface waters and to identify STPs for

which more advanced treatment might be required and to protect EU aquatic biodiversity. This study did not aim to assess what advanced treatment should be implemented. The most suitable treatment technique depends on a multitude of factors and will most likely be location specific. For example, ozonation may result in the formation of toxic by-products, which is why a post-treatment step with a biological active sand filter is recommended (von Gunten, 2018). On the other hand, ozonation is unlike activated carbon treatment effective in the inactivation of bacteria. Consequently, when stringent limits for reuse are requested, an additional disinfection step might be needed for when activated carbon is implemented. In addition, other environmental burdens than risks of chemicals need to be assessed. Treatment with

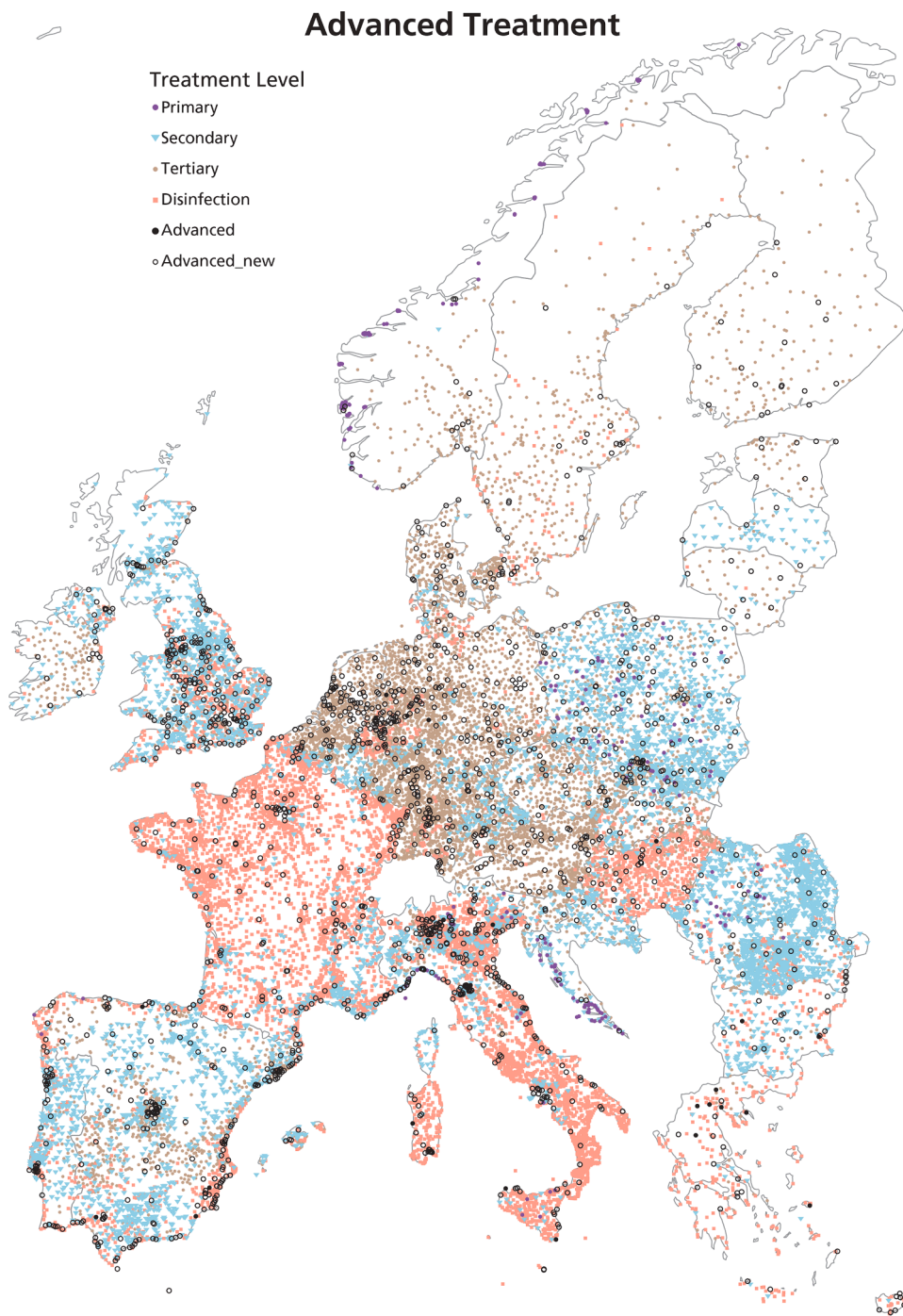


Fig. 6. STPs and their treatment level under the Advanced Treatment Scenario. The large STPs that will be upgraded with advanced treatment are shown in the figure as Advanced_new.

ozonation is for example associated with higher environmental impacts due to its high energy consumption (Ganora et al., 2019; Pistocchi et al., 2022c). One of the aims laid down in the UWWTD proposal is to achieve energy neutrality in the wastewater sector by 2040 (European Commission, 2022b). The use of renewable energy resources might help achieve this aim and lower the negative impacts of advanced treatments (Lutterbeck et al., 2020). All this emphasises the need for integrated assessments before deciding whether an STP needs to be updated with advanced treatment (Pistocchi et al., 2017; Schuwirth et al., 2018).

4. Conclusion

Treatment of wastewater is a key component to reduce environmental emissions of pharmaceuticals. Here, we showed that implementing advanced treatment at STPs with a capacity of >100.000 p.e. will improve the total pharmaceutical emission reduction potential of STPs in Europe from 48% to 69% based on a set of 58 priority pharmaceuticals. This set of the 58 pharmaceuticals was based on existing prioritisation lists and covers a wide variety of (physical-chemical) properties and different use categories. Average STP removal efficiencies ranged from 9% for primary treatment to 84% for advanced treatment. The data collected in this study can be complemented with

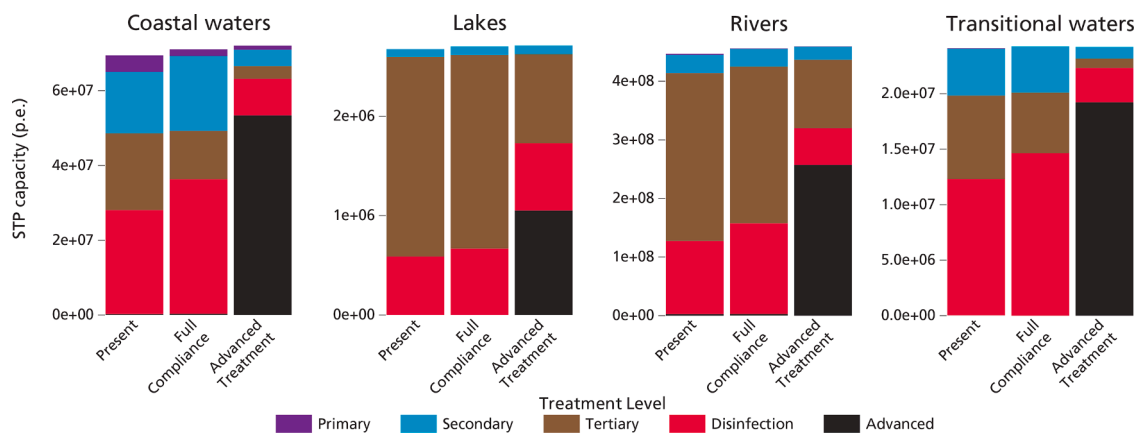


Fig. 7. Total amount of treated STP effluent (in p.e.) per that is emitted into coastal waters, lakes, rivers and transitional waters (waters between land and sea, including fjords, estuaries, lagoons and deltas) under the Present, Full Compliance and Advanced Treatment scenarios.

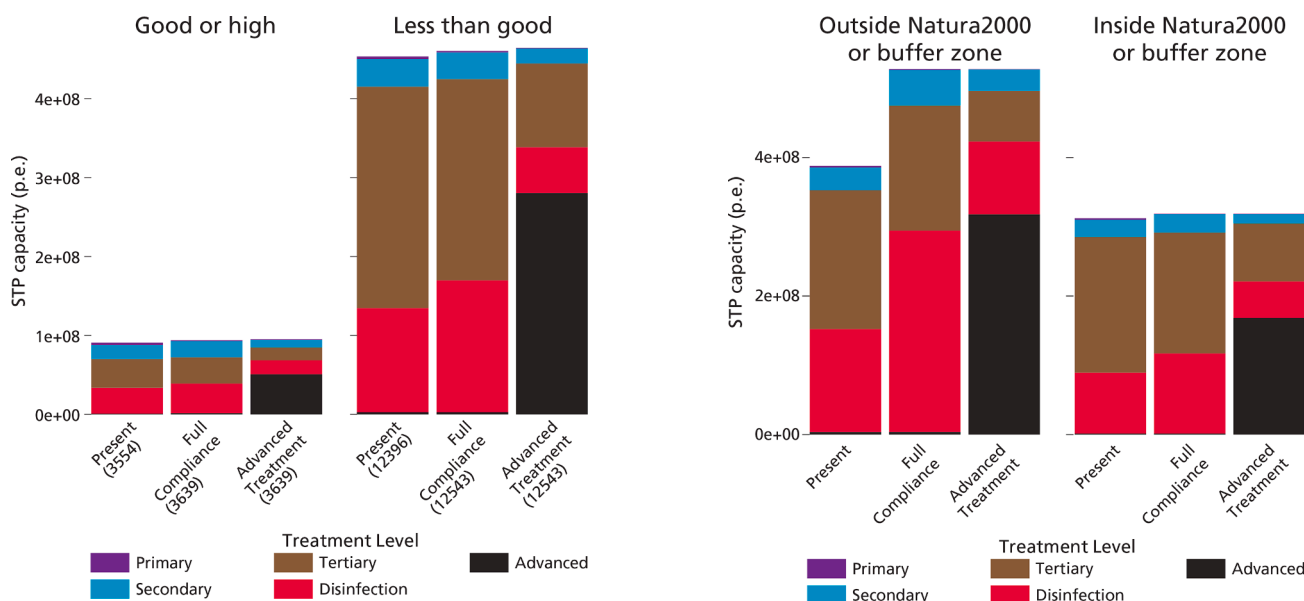


Fig. 8. European wide analysis of the total STP capacity (in p.e.) per treatment level that emits into water bodies with a good or less than good ecological status as assessed under the WFD. Total number of water bodies are shown in brackets.

Fig. 9. European wide analysis of the total STP capacity (in p.e.) per treatment level that is emitted outside or inside a Natura2000 area or the 2.000 m buffer zone under the Present, Full Compliance and Advanced Treatment scenarios.

other substance types, such as biocides and REACH registered chemicals, and consumption data to obtain a better understanding of the total chemical pressure on water bodies.

Spatial differences with regard to implemented STP treatment levels exist under all three scenarios. Coastal waters and lakes seem for example not as well protected as freshwaters, whilst some of these coastal waters have already a less than good ecological status or potential. Furthermore, more stringent treatment for STPs near Natura2000 sites and STPs that emit effluent into water bodies with a less than good ecological status was not observed but might be required to protect biodiversity. This study did not aim to assess what advanced treatment should be implemented and to define which specific STPs need to be upgraded as the most suitable water management option depends on a multitude of factors and will most likely be location specific. Integrated assessments are needed that estimate total environmental benefits and burdens of STP treatments, as well as other relevant parameters such as costs in order to decide on water management practices and to achieve long-term environmental goals listed under e.g. the WFD and (revised) UWWTD.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data that supports the findings of this study are openly available in Mendely Data at <https://data.mendeley.com/datasets/zsrv92557p>.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.watres.2023.120157](https://doi.org/10.1016/j.watres.2023.120157).

References

- Adeleye, A.S., Xue, J., Zhao, Y., Taylor, A.A., Zenobio, J.E., Sun, Y., Han, Z., Salawu, O. A., Zhu, Y., 2022. Abundance, fate, and effects of pharmaceuticals and personal care products in aquatic environments. *J. Hazard. Mater.* 424, 127284 <https://doi.org/10.1016/j.jhazmat.2021.127284>.
- aus der Beek, T., Weber, F.-A., Bergmann, A., Hickmann, S., Ebert, L., Hein, A., Küster, A., 2016. Pharmaceuticals in the environment—Global occurrences and perspectives. *Environmen. Toxicol. Chem.* 35, 823–835. <https://doi.org/10.1002/etc.3339>.
- Belloni, A., Morgan, D., Paris, V., 2016. Pharmaceutical expenditure and policies: past trends and future challenges.
- Bernhardt, E.S., Rosi, E.J., Gessner, M.O., 2017. Synthetic chemicals as agents of global change. *Front. Ecol. Environ* 15, 84–90. <https://doi.org/10.1002/fee.1450>.
- Birk, S., Chapman, D., Carvalho, L., Spears, B.M., Andersen, H.E., Argillier, C., Auer, S., Baattrup-Pedersen, A., Banin, L., Beklioglu, M., Bondar-Kunze, E., Borja, A., Branco, P., Bucak, T., Buijse, A.D., Cardoso, A.C., Couture, R.-M., Cremona, F., de Zwart, D., Feld, C.K., Ferreira, M.T., Feuchtmayr, H., Gessner, M.O., Gieswein, A., Globevnik, L., Graeber, D., Graf, W., Gutiérrez-Cánovas, C., Hanganu, J., Işkan, U., Järvinen, M., Jeppesen, E., Kotamäki, N., Kuijper, M., Lemm, J.U., Lu, S., Solheim, A. L., Mischke, U., Moe, S.J., Nøges, P., Nøges, T., Ormerod, S.J., Panagopoulos, Y., Phillips, G., Posthuma, L., Pouso, S., Prudhomme, C., Rankinen, K., Rasmussen, J.J., Richardson, J., Sagouis, A., Santos, J.M., Schäfer, R.B., Schinegger, R., Schmutz, S., Schneider, S.C., Schilling, L., Segurado, P., Stefanidis, K., Sures, B., Thackeray, S.J., Turunen, J., Uyarra, M.C., Venohr, M., von der Ohe, P.C., Willby, N., Hering, D., 2020. Impacts of multiple stressors on freshwater biota across spatial scales and ecosystems. *Nat. Ecol. Evol.* 4, 1060–1068. <https://doi.org/10.1038/s41559-020-1216-4>.
- Boretti, A., Rosa, L., 2019. Reassessing the projections of the World Water Development Report. *npj Clean Water* 2, 1–6. <https://doi.org/10.1038/s41545-019-0039-9>.
- Bunke, D., Moritz, S., Brack, W., Herráez, D.L., Posthuma, L., Nuss, M., 2019. Developments in society and implications for emerging pollutants in the aquatic environment. *Environmen. Sci. Europe* 31, 32. <https://doi.org/10.1186/s12302-019-0213-1>.
- Carvalho, L., Mackay, E.B., Cardoso, A.C., Baattrup-Pedersen, A., Birk, S., Blackstock, K. L., Borics, G., Borja, A., Feld, C.K., Ferreira, M.T., Globevnik, L., Grizzetti, B., Hendry, S., Hering, D., Kelly, M., Langaas, S., Meissner, K., Panagopoulos, Y., Penning, E., Rouillard, J., Sabater, S., Schmedtje, U., Spears, B.M., Venohr, M., van de Bund, W., Solheim, A.L., 2019. Protecting and restoring Europe's waters: an analysis of the future development needs of the Water Framework Directive. *Sci. Total Environ.* 658, 1228–1238. <https://doi.org/10.1016/j.scitotenv.2018.12.255>.
- Collivignarelli, M.C., Abbà, A., Alloisio, G., Gozio, E., Benigna, I., 2017. Disinfection in wastewater treatment plants: evaluation of effectiveness and acute toxicity effects. *Sustainability* 9, 1704. <https://doi.org/10.3390/su9101704>.
- Comber, S., Gardner, M., Jones, V., Ellor, B., 2015. Source apportionment of trace contaminants in urban sewer catchments. *Environ. Technol.* 36, 573–587. <https://doi.org/10.1080/09593330.2014.953599>.
- Coppens, L.J.C., van Gils, J.A.G., ter Laak, T.L., Raterman, B.W., van Wezel, A.P., 2015. Towards spatially smart abatement of human pharmaceuticals in surface waters: defining impact of sewage treatment plants on susceptible functions. *Water Res.* 81, 356–365. <https://doi.org/10.1016/j.watres.2015.05.061>.
- de Voogt, P., Janex-Habibi, M.-L., Sacher, F., Puijker, L., Mons, M., 2009. Development of a common priority list of pharmaceuticals relevant for the water cycle. *Water Sci. Technol.* 59, 39–46. <https://doi.org/10.2166/wst.2009.764>.
- Dingemans, M.M.L., Smeets, P.W.M.H., Medema, G., Frijns, J., Raat, K.J., van Wezel, A. P., Bartholomeus, R.P., 2020. Responsible water reuse needs an interdisciplinary approach to balance risks and benefits. *Water (Basel)* 12, 1264. <https://doi.org/10.3390/w12051264>.
- EEA, 2022a. Waterbase-UWWTD [WWW Document]. URL https://www.eea.europa.eu/ds_resolveuid/3634d42426e846579594dd20928ccc26.
- EEA, 2022b. Natura 2000 data - the European network of protected sites. Prod-ID: DAT-68-en.
- EEA, 2021. WISE Water framework directive database. Prod-ID: DAT-124-en.
- EEA, 2018a. European waters: assessment of status and pressures 2018. EEA Report No 7/2018.
- EEA, 2018b. Natura 2000 buffer zones [WWW Document]. URL https://www.eea.europa.eu/ds_resolveuid/ed23d812841549e39b937d1043441b6a (accessed 10.18.22).
- EEA, 2017. Indicator Assessment: urban waste water treatment in Europe [WWW Document]. URL <https://www.eea.europa.eu/data-and-maps/indicators/urban-waste-water-treatment/urban-waste-water-treatment-assessment-4> (accessed 2.2.22).
- European Commission, 2022a. COMMISSION IMPLEMENTING DECISION (EU) 2022/1307 of 22 July 2022 establishing a watch list of substances for Union-wide monitoring in the field of water policy pursuant to Directive 2008/105/EC of the European Parliament and of the Council (notified under document C(2022) 5098) (Text with EEA relevance).
- European Commission, 2022b. Proposal for a DIRECTIVE OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL concerning urban wastewater treatment (recast) (Text with EEA relevance) (SEC(2022) 541) - (SWD(2022) 541, 544) (No. COM(2022) 541 final). Brussels. Belgium.
- European Commission, 2022c. 11th technical assessment on UWWTD implementation. European overview & national situation.
- European Commission, 2022d DRAFT: COMMISSION DELEGATED REGULATION (EU) .../... of XXX amending Regulation (EC) No 1272/2008 as regards hazard classes and criteria for the classification, labelling and packaging of substances and mixtures (Text with EEA relevance). Ref. Ares(2022)6485391 - 20/09/2022.
- European Commission, 2020a. COM(2020) 380 final. Communication From The Commission To The European Parliament, The Council, The European Economic And Social Committee And The Committee Of The Regions EU. Biodiversity Strategy For 2030. Bringing nature Back Into Our Lives. Brussels. Belgium.
- European Commission, 2020b. Communication from the commission to the european parliament, the council, the european economic and social committee and the committee of the regions Pharmaceutical Strategy for Europe (SWD(2020) 286 final).
- European Commission, 2020c. Commission Implementing Decision (EU) 2020/1161 of 4 August 2020 establishing a watch list of substances for Union-wide monitoring in the field of water policy pursuant to Directive 2008/105/EC of the European Parliament and of the Council (notified under document number C(2020) 5205) (Text with EEA relevance).
- Eurostat, 2022. Population connected to wastewater treatment plants (ENV_WW_CON) [WWW Document]. URL https://ec.europa.eu/eurostat/databrowser/view/ENV_WW_CON_custom_2896246/default?tabu?lang=en (accessed 1.5.22).
- Fabbri, E., Franzellitti, S., 2016. Human pharmaceuticals in the marine environment: focus on exposure and biological effects in animal species. *Environmen. Toxicol. Chem.* 35, 799–812.
- Fischer, A., van Wezel, A.P., Hollender, J., Cornelissen, E., Hofman, R., Peter van der Hoek, J., 2019. Development and application of relevance and reliability criteria for water treatment removal efficiencies of chemicals of emerging concern. *Water Res.* <https://doi.org/10.1016/j.watres.2019.05.088>.
- FOEN, 2015. Gewässerqualität: revision der Gewässerschutzverordnung [WWW Document]. URL <https://www.bafu.admin.ch/bafu/de/home/themen/bildung/mgdiennmitteilungen.msg-id-59323.html> (accessed 6.14.22).
- Ganora, D., Hospido, A., Husemann, J., Krampe, J., Loderer, C., Longo, S., Bouyat, L.M., Obermaier, N., Piraccini, E., Stanev, S., Váci, L., Pistocchi, A., 2019. Opportunities to improve energy use in urban wastewater treatment: a European-scale analysis. *Environ. Res. Lett.* 14, 044028 <https://doi.org/10.1088/1748-9326/ab0b54>.
- Gollong, G., Neuwald, I.J., Kuckelkorn, J., Junek, R., Zahn, D., 2022. Assessing the protection gap for mobile and persistent chemicals during advanced water treatment – A study in a drinking water production and wastewater treatment plant. *Water Res.* 221, 118847 <https://doi.org/10.1016/j.watres.2022.118847>.
- Greenham, R.T., Miller, K.Y., Tong, A., 2019. Removal efficiencies of top-used pharmaceuticals at sewage treatment plants with various technologies. *J. Environmen. Chem. Engin.* 7, 103294 <https://doi.org/10.1016/j.jece.2019.103294>.
- Grizzetti, B., Lique, C., Pistocchi, A., Vigiak, O., Zulian, G., Bouraoui, F., De Roo, A., Cardoso, A.C., 2019. Relationship between ecological condition and ecosystem services in European rivers, lakes and coastal waters. *Sci. Total Environ.* 671, 452–465. <https://doi.org/10.1016/j.scitotenv.2019.03.155>.
- Hale, S.E., Neumann, M., Schliebner, I., Schulze, J., Averbek, F.S., Castell-Exner, C., Collard, M., Drmač, D., Hartmann, J., Hofman-Caris, R., Hollender, J., de Jonge, M., Kullick, T., Lennquist, A., Letzel, T., Nödler, K., Pawlowski, S., Reineke, N., Rorije, E., Scheurer, M., Sigmund, G., Timmer, H., Trier, X., Verbruggen, E., Arp, H. P.H., 2022. Getting in control of persistent, mobile and toxic (PMT) and very persistent and very mobile (vPvM) substances to protect water resources: strategies from diverse perspectives. *Environmen. Sci. Europe* 34, 22. <https://doi.org/10.1186/s12302-022-00604-4>.
- Herrmann, M., Olsson, O., Fiehn, R., Herrel, M., Kümmerer, K., 2015. The significance of different health institutions and their respective contributions of active pharmaceutical ingredients to wastewater. *Environ. Int* 85, 61–76. <https://doi.org/10.1016/j.envint.2015.07.020>.
- Houtman, C.J., Kroesbergen, J., Lekkerkerker-Teunissen, K., van der Hoek, J.P., 2014. Human health risk assessment of the mixture of pharmaceuticals in Dutch drinking water and its sources based on frequent monitoring data. *Sci. Total Environ.* 496, 54–62. <https://doi.org/10.1016/j.scitotenv.2014.07.022>.
- Ikehata, K., Jodeiri Naghashkar, N., Gamal El-Din, M., 2006. Degradation of aqueous pharmaceuticals by Ozonation and advanced oxidation processes: a review. *Ozone* 28, 353–414. <https://doi.org/10.1080/01919510600985937>.
- Khetan, S.K., Collins, T.J., 2007. Human pharmaceuticals in the aquatic environment: a challenge to green chemistry. *Chem. Rev.* 107, 2319–2364. <https://doi.org/10.1021/cr020441w>.
- Klein, E.Y., Van Boeckel, T.P., Martinez, E.M., Pant, S., Gandra, S., Levin, S.A., Goossens, H., Laxminarayan, R., 2018. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proceed. National Acad. Sci.* 115, E3463–E3470. <https://doi.org/10.1073/pnas.1717295115>.
- Kosek, K., Luczkiewicz, A., Fudala-Książek, S., Jankowska, K., Szopińska, M., Svahn, O., Tränckner, J., Kaiser, A., Langas, V., Björklund, E., 2020. Implementation of advanced micropollutants removal technologies in wastewater treatment plants (WWTPs) - Examples and challenges based on selected EU countries. *Environ. Sci. Policy* 112, 213–226. <https://doi.org/10.1016/j.envsci.2020.06.011>.
- Kümmerer, K., Dionysiou, D.D., Olsson, O., Fatta-Kassinos, D., 2019. Reducing aquatic micropollutants – increasing the focus on input prevention and integrated emission management. *Sci. Total Environ.* 652, 836–850. <https://doi.org/10.1016/j.scitotenv.2018.10.219>.
- Kümmerer, K., Dionysiou, D.D., Olsson, O., Fatta-Kassinos, D., 2018. A path to clean water. *Science* 361, 222–224. <https://doi.org/10.1126/science.aau2405>.

- Lautz, L.S., Struijs, J., Nolte, T.M., Breure, A.M., van der Grinten, E., van de Meent, D., van Zelm, R., 2017. Evaluation of SimpleTreat 4.0: simulations of pharmaceutical removal in wastewater treatment plant facilities. *Chemosphere* 168, 870–876. <https://doi.org/10.1016/j.chemosphere.2016.10.123>.
- Le Corre, K.S., Ort, C., Katelye, D., Allen, B., Escher, B.I., Keller, J., 2012. Consumption-based approach for assessing the contribution of hospitals towards the load of pharmaceutical residues in municipal wastewater. *Environ. Int* 45, 99–111. <https://doi.org/10.1016/j.envint.2012.03.008>.
- Lemm, J.U., Feld, C.K., Birk, S., 2019. Diagnosing the causes of river deterioration using stressor-specific metrics. *Sci. Total Environ.* 651, 1105–1113. <https://doi.org/10.1016/j.scitotenv.2018.09.157>.
- Lemm, J.U., Venohr, M., Globevnik, L., Stefanidis, K., Panagopoulos, Y., van Gils, J., Posthuma, L., Kristensen, P., Feld, C.K., Mahnkopf, J., Hering, D., Birk, S., 2021. Multiple stressors determine river ecological status at the European scale: towards an integrated understanding of river status deterioration. *Glob. Chang. Biol* 27, 1962–1975. <https://doi.org/10.1111/gcb.15504>.
- Logar, I., Brouwer, R., Maurer, M., Ort, C., 2014. Cost-benefit analysis of the Swiss national policy on reducing micropollutants in treated wastewater. *Environ. Sci. Technol.* 48, 12500–12508. <https://doi.org/10.1021/es502338j>.
- Luo, Y., Guo, W., Ngo, H.H., Nghiem, L.D., Hai, F.I., Zhang, J., Liang, S., Wang, X.C., 2014. A review on the occurrence of micropollutants in the aquatic environment and their fate and removal during wastewater treatment. *Sci. Total Environ.* 473–474, 619–641. <https://doi.org/10.1016/j.scitotenv.2013.12.065>.
- Lutterbeck, C.A., Colares, G.S., Dell'Osbel, N., da Silva, F.P., Kist, L.T., Machado, Ê.L., 2020. Hospital laundry wastewaters: a review on treatment alternatives, life cycle assessment and prognosis scenarios. *J. Clean. Prod* 273, 122851. <https://doi.org/10.1016/j.jclepro.2020.122851>.
- Massei, R., Busch, W., Wolschke, H., Schinkel, L., Bitsch, M., Schulze, T., Krauss, M., Brack, W., 2018. Screening of pesticide and biocide patterns as risk drivers in sediments of major European river mouths: ubiquitous or river basin-specific contamination? *Environ. Sci. Technol.* 52, 2251–2260. <https://doi.org/10.1021/acs.est.7b04355>.
- McLachlan, M.S., Li, Z., Jonsson, L., Kaserzon, S., O'Brien, J.W., Mueller, J.F., 2022. Removal of 293 organic compounds in 15 WWTPs studied with non-targeted suspect screening. *Environ. Sci. Res.* 8, 1423–1433. <https://doi.org/10.1039/D2EW00088A>.
- Mezzelani, M., Gorbi, S., Regoli, F., 2018. Pharmaceuticals in the aquatic environments: evidence of emerged threat and future challenges for marine organisms. *Mar. Environ. Res.* 140, 41–60. <https://doi.org/10.1016/j.marenvres.2018.05.001>.
- Michael, I., Rizzo, L., McArdell, C.S., Manaia, C.M., Merlin, C., Schwartz, T., Dagot, C., Fatta-Kassinos, D., 2013. Urban wastewater treatment plants as hotspots for the release of antibiotics in the environment: a review. *Water Res.* 47, 957–995. <https://doi.org/10.1016/j.watres.2012.11.027>.
- Nagesh, P., de Boer, H.J., van Wezel, A.P., Dekker, S.C., van Vuuren, D.P., 2022. Development of chemical emission scenarios using the Shared Socio-economic Pathways. *Sci. Total Environ.* 836, 155530. <https://doi.org/10.1016/j.scitotenv.2022.155530>.
- NORMAN Network, 2014. NORMAN Proposal For Candidate Substances For the 1st EU Watch List (Art 8 Ter of 2013/39/EU Directive). Working Group Prioritisation.
- OECD, 2021. Health at a Glance 2021: OECD Indicators. Pharmaceutical consumption [WWW Document]. URL <https://www.oecd-ilibrary.org/sites/5689c05c-en/index.html?itemId=/content/component/5689c05c-en>.
- OECD, 2019. Pharmaceutical Residues in Freshwater: Hazards and Policy Responses. OECD Studies on Water.
- OECD, 2003. Glossary of statistical terms [WWW Document]. URL <https://stats.oecd.org/glossary/index.htm> (accessed 2.2.22).
- Oldenkamp, R., Hoeks, S., Cengic, M., Barbarossa, V., Burns, E.E., Boxall, A.B.A., Rags, A.M.J., 2018. A high-resolution spatial model to predict exposure to pharmaceuticals in European surface waters: ePIE. *Environ. Sci. Technol.* 52, 12494–12503. <https://doi.org/10.1021/acs.est.8b03862>.
- Pistocchi, Alberto, Alygizakis, N.A., Brack, W., Boxall, A., Cousins, I.T., Drewes, J.E., Finckh, S., Gallé, T., Launay, M.A., McLachlan, M.S., Petrovic, M., Schulze, T., Slobodnik, J., Ternes, T., Van Wezel, A., Verlicchi, P., Whalley, C., 2022a. European scale assessment of the potential of ozonation and activated carbon treatment to reduce micropollutant emissions with wastewater. *Sci. Total Environ.* 157124. <https://doi.org/10.1016/j.scitotenv.2022.157124>.
- Pistocchi, A., Andersen, H.R., Bertanza, G., Brander, A., Choubert, J.M., Cimbritz, M., Drewes, J.E., Koehler, C., Krampe, J., Launay, M., Nielsen, P.H., Obermaier, N., Stanev, S., Thornberg, D., 2022c. Treatment of micropollutants in wastewater: balancing effectiveness, costs and implications. *Sci. Total Environ.* 850, 157593. <https://doi.org/10.1016/j.scitotenv.2022.157593>.
- Pistocchi, A., Parravicini, V., Langergraber, G., Masi, F., 2022b. How many small agglomerations do exist in the European union, and how should we treat their wastewater? *Water Air Soil Pollut* 233, 431. <https://doi.org/10.1007/s11270-022-05880-7>.
- Pistocchi, A., Udias, A., Grizzetti, B., Gelati, E., Koundouri, P., Ludwig, R., Papandreou, A., Souliotis, I., 2017. An integrated assessment framework for the analysis of multiple pressures in aquatic ecosystems and the appraisal of management options. *Sci. Total Environ.* 575, 1477–1488. <https://doi.org/10.1016/j.scitotenv.2016.10.020>.
- Pomies, M., Choubert, J.M., Wisniewski, C., Coquery, M., 2013. Modelling of micropollutant removal in biological wastewater treatments: a review. *Sci. Total Environ.* 443, 733–748. <https://doi.org/10.1016/j.scitotenv.2012.11.037>.
- Posthuma, L., Brown, C.D., de Zwart, D., Diamond, J., Dyer, S.D., Holmes, C.M., Marshall, S., Burton, G.A., 2018. Prospective mixture risk assessment and management prioritizations for river catchments with diverse land uses. *Environmen. Toxicol. Chem.* 37, 715–728. <https://doi.org/10.1002/etc.3960>.
- Pronk, T.E., Hofman-Caris, R.C.H.M., Vries, D., Kools, S.A.E., ter Laak, T.L., Stroomberg, G.J., 2020. A water quality index for the removal requirement and purification treatment effort of micropollutants. *Water Supply* 21, 128–145. <https://doi.org/10.2166/ws.2020.289>.
- Puhlmann, N., Mols, R., Olsson, O., Chris Slootweg, J., Kümmerer, K., 2021. Towards the design of active pharmaceutical ingredients mineralizing readily in the environment. *Green Chem.* 23, 5006–5023. <https://doi.org/10.1039/D1GC01048D>.
- Reid, A.J., Carlson, A.K., Creed, I.F., Eliason, E.J., Gell, P.A., Johnson, P.T.J., Kidd, K.A., MacCormack, T.J., Olden, J.D., Ormerod, S.J., Smol, J.P., Taylor, W.W., Tockner, K., Vermaire, J.C., Dudgeon, D., Cooke, S.J., 2019. Emerging threats and persistent conservation challenges for freshwater biodiversity. *Biolog. Rev.* 94, 849–873. <https://doi.org/10.1111/brv.12480>.
- Rout, P.R., Zhang, T.C., Bhunia, P., Surampalli, R.Y., 2021. Treatment technologies for emerging contaminants in wastewater treatment plants: a review. *Sci. Total Environ.* 753, 141990. <https://doi.org/10.1016/j.scitotenv.2020.141990>.
- Schulze, S., Zahn, D., Montes, R., Rodil, R., Quintana, J.B., Knepper, T.P., Reemtsma, T., Berger, U., 2019. Occurrence of emerging persistent and mobile organic contaminants in European water samples. *Water Res.* 80–90. <https://doi.org/10.1016/j.watres.2019.01.008>.
- Schuwirth, N., Honti, M., Logar, I., Stamm, C., 2018. Multi-criteria decision analysis for integrated water quality assessment and management support. *Water Res.* X (1), 100010. <https://doi.org/10.1016/j.wroa.2018.100010>.
- Sjerps, R., Brunner, A.M., Fujita, Y., Bajema, B., de Jonge, M., Bäuerlein, P.S., de Munk, J., Schriks, M., van Wezel, A., 2021. Clustering and prioritization to design a risk-based monitoring program in groundwater sources for drinking water. *Environmen. Sci. Europe* 33, 1–13.
- Stamm, C., Eggen, R.I.L., Hering, J.G., Hollender, J., Joss, A., Schärer, M., 2015. Micropollutant removal from wastewater: facts and decision-making despite uncertainty. *Environ. Sci. Technol.* 49, 6374–6375. <https://doi.org/10.1021/acs.est.5b02242>.
- Straub, J.O., 2016. Reduction in the environmental exposure of pharmaceuticals through diagnostics, Personalised Healthcare and other approaches. A mini review and discussion paper. *Sustain. Chem. Pharm.* 3, 1–7. <https://doi.org/10.1016/J.SCP.2015.12.001>.
- Struijs, J., 2014. SimpleTreat 4.0: a Model to Predict Fate and Emission of Chemicals in Wastewater Treatment plants: Background Report Describing the Equations (No. RIVM Report 601353005/2014). Rijksinstituut voor Volksgezondheid en Milieu, Bilthoven, the Netherlands.
- van Dijk, J., Dekker, S.C., Kools, S.A., Van Wezel, A.P., 2023. Data for: "European-wide spatial analysis of sewage treatment plants and the possible benefits to nature of advanced treatment to reduce pharmaceutical emissions. V2. Mendeley. Data. 2. <https://doi.org/10.17632/zsr92557p.2>.
- van Gils, J., Posthuma, L., Cousins, I.T., Brack, W., Altenburger, R., Baveco, H., Focks, A., Greskowiak, J., Kühne, R., Kutsarova, S., Lindim, C., Markus, A., van de Meent, D., Munthe, J., Schueder, R., Schüürmann, G., Slobodnik, J., de Zwart, D., van Wezel, A., 2020. Computational material flow analysis for thousands of chemicals of emerging concern in European waters. *J. Hazard. Mater.* <https://doi.org/10.1016/j.jhazmat.2020.122655>, 122655–122655.
- van Gils, J., Posthuma, L., Cousins, I.T., Lindim, C., de Zwart, D., Bunke, D., Kutsarova, S., Müller, C., Munthe, J., Slobodnik, J., Brack, W., 2019. The European Collaborative Project SOLUTIONS developed models to provide diagnostic and prognostic capacity and fill data gaps for chemicals of emerging concern. *Environmen. Sci. Europe* 31, 1–8. <https://doi.org/10.1186/s12302-019-0248-3>.
- Villarrín, M.C., Merel, S., 2020. Paradigm shifts and current challenges in wastewater management. *J. Hazard. Mater.* 390. <https://doi.org/10.1016/j.jhazmat.2020.122139>, 122139–122139.
- von Gunten, U., 2018. Oxidation processes in water treatment: are we on track? *Environ. Sci. Technol.* 52, 5062–5075. <https://doi.org/10.1021/acs.est.8b00586>.
- Wezel, A.P.V., Laak, T.L.T., Fischer, A., Bäuerlein, P.S., Munthe, J., Posthuma, L., Wezel, A.P.V., Laak, T.L.T., Fischer, A., Bäuerlein, P.S., Munthe, J., Posthuma, L., 2017. Mitigation options for chemicals of emerging concern in surface waters; operationalising solutions-focused risk assessment 3, 403–414. <https://doi.org/10.1039/c7ew00077d>.
- Wilkinson, J.L., Boxall, A.B.A., Kolpin, D.W., Leung, K.M.Y., Lai, R.W.S., Galbán-Malagón, C., Adell, A.D., Mondon, J., Metian, M., Marchant, R.A., Bouzas-Monroy, A., Cuni-Sanchez, A., Coors, A., Carriquiriborde, P., Rojo, M., Gordon, C., Cara, M., Moermond, M., Luarte, P., Petrosyan, V., Perikhanian, Y., Mahon, C.S., McGurk, C.J., Hofmann, T., Kormoker, T., Iniguez, V., Guzman-Otazo, J., Tavares, J. L., Figueiredo, F.G.D., Razzolini, M.T.P., Dougnon, V., Gbaguidi, G., Traoré, O., Blais, J.M., Kimpe, L.E., Wong, M., Wong, D., Ntchantcho, R., Pizarro, J., Ying, G.-G., Chen, C.-E., Páez, M., Martínez-Lara, J., Otamonga, J.-P., Poté, J., Ifo, S.A., Wilson, P., Echeverría-Sáenz, S., Udikovic-Kolic, N., Milakovic, M., Fatta-Kassinos, D., Ioannou-Ttola, L., Belušová, V., Vymazal, J., Cárdenas-Bustamante, M., Kassa, B.A., Garric, J., Chaumot, A., Gibbs, P., Kunchulia, I., Seidensticker, S., Lyberatos, G., Halldórsson, H.P., Mellinger, M., Shashidhar, T., Lamba, M., Nastiti, A., Supriatin, A., Pourang, N., Abedini, A., Abdullah, O., Gharbia, S.S., Pilla, F., Chefetz, B., Topaz, T., Yao, K.M., Aubakirova, B., Beisenova, R., Olaka, L., Mulu, J. K., Chatanga, P., Ntuli, V., Blama, N.T., Sherif, S., Aris, A.Z., Looi, L.J., Niang, M., Traore, S.T., Oldenkamp, R., Ogunbanwo, O., Ashfaq, M., Iqbal, M., Abdeen, Z., O'Dea, A., Morales-Saldaña, J.M., Custodio, M., Cruz, H.de la, Navarrete, I., Carvalho, F., Gogra, A.B., Koroma, B.M., Cerkenvik-Flajs, V., Gombáč, M., Thwala, M., Choi, K., Kang, H., Ladu, J.L.C., Rico, A., Amerasinghe, P., Sobek, A., Horlitz, G., Zenker, A.K., King, A.C., Jiang, J.-J., Kariuki, R., Tumbo, M., Tezel, U., Onay, T.T., Lejju, J.B., Vystavna, Y., Vergeles, Y., Heinzen, H., Pérez-Parada, A.,

- Sims, D.B., Figy, M., Good, D., Teta, C., 2022. Pharmaceutical pollution of the world's rivers. PNAS 119. <https://doi.org/10.1073/pnas.2113947119>.
- Yang, Y., Ok, Y.S., Kim, K.-H., Kwon, E.E., Tsang, Y.F., 2017. Occurrences and removal of pharmaceuticals and personal care products (PPCPs) in drinking water and water/sewage treatment plants: a review. Sci. Total Environ. 596–597, 303–320. <https://doi.org/10.1016/j.scitotenv.2017.04.102>.
- Zhou, S., Di Paolo, C., Wu, X., Shao, Y., Seiler, T.-B., Hollert, H., 2019. Optimization of screening-level risk assessment and priority selection of emerging pollutants – The case of pharmaceuticals in European surface waters. Environ. Int 128, 1–10. <https://doi.org/10.1016/j.envint.2019.04.034>.