

# Assessing the burden of antibiotics and other pharmaceuticals in the water cycle from anthropogenic and animal farms sources

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**IMN** ISTITUTO DI RICERCHE  
FARMACOLOGICHE  
MARIO NEGRI · IRCCS

# Farmaci nell'ambiente – Fonti di Immissione

Pharmaceuticals are **ubiquitous contaminants** in the environment

## Human Use

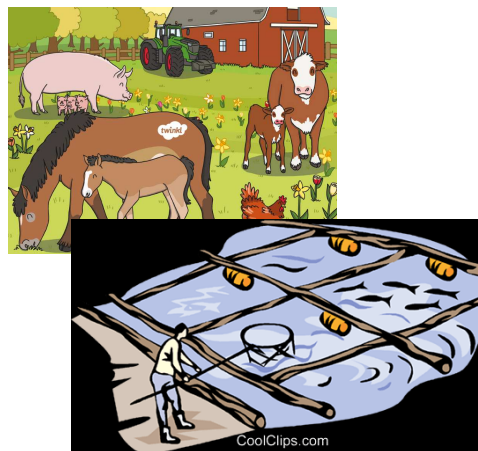
### Wastewater Treatment Plants Effluents



### Direct discharge of wastewater



## Veterinary Use



### Animal farms and aquaculture

## Industrial discharge



### Local contamination

**Active** compounds in complex **mixtures**

# Pharmaceuticals in the environment

RESEARCH LETTERS

## Presence of therapeutic drugs in the environment

*Ettore Zuccato, Davide Calamari, Marco Natangelo, Roberto Fanelli*

Therapeutic drugs can contaminate the environment because of metabolic excretion, improper disposal, or industrial waste. To assess the extent of this contamination, we listed drugs thought to be putative priority pollutants according to selected criteria, and measured them in Lombardy, Italy. Most drugs were measurable in drinking or river waters and sediments, suggesting that pharmaceutical products are widespread contaminants, with possible implications for human health and the environment.

**The Lancet, 2000, 355, 1789-1790**

**First Monitoring** of pharmaceuticals in surface and tap water in Italy

**Mass balance** of pharmaceuticals in surface water in Italy

## Removal of Pharmaceuticals in Sewage Treatment Plants in Italy

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ROBERTO FANELLI,<sup>‡</sup>  
FRANCESCO POMATI,<sup>†</sup>  
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**Environmental Science and Technology, 2006, 407, 357-363**

Monitoring **fate and removal** of pharmaceuticals and antibiotics

Source, occurrence and fate of antibiotics in the Italian aquatic environment

Ettore Zuccato\*, Sara Castiglioni, Renzo Bagnati, Manuela Melis, Roberto Fanelli

*Department of Environmental Health Sciences, Mario Negri Institute for Pharmacological Research, Via La Masa 19, 20156 Milan, Italy*

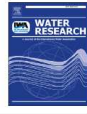
**Journal of Hazardous Materials, 2010, 179, 1042-1048**

## Strategic Survey of Therapeutic Drugs in the Rivers Po and Lambro in Northern Italy

DAVIDE CALAMARI,<sup>†,‡</sup>  
ETTORE ZUCCATO,<sup>†</sup>  
SARA CASTIGLIONI,<sup>†,‡</sup>  
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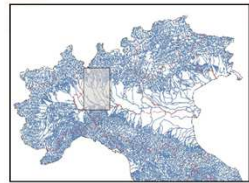
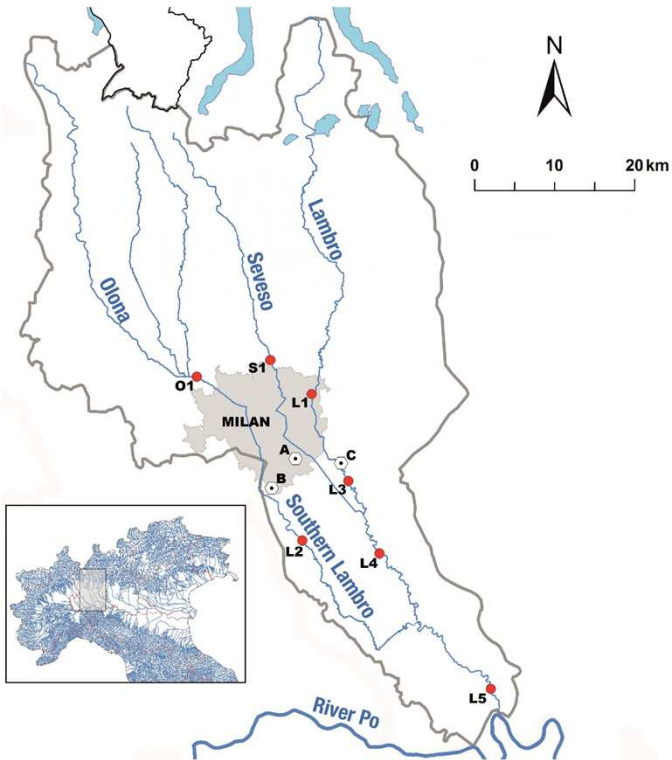
**Environmental Science and Technology, 2003, 37, 1241-1248**



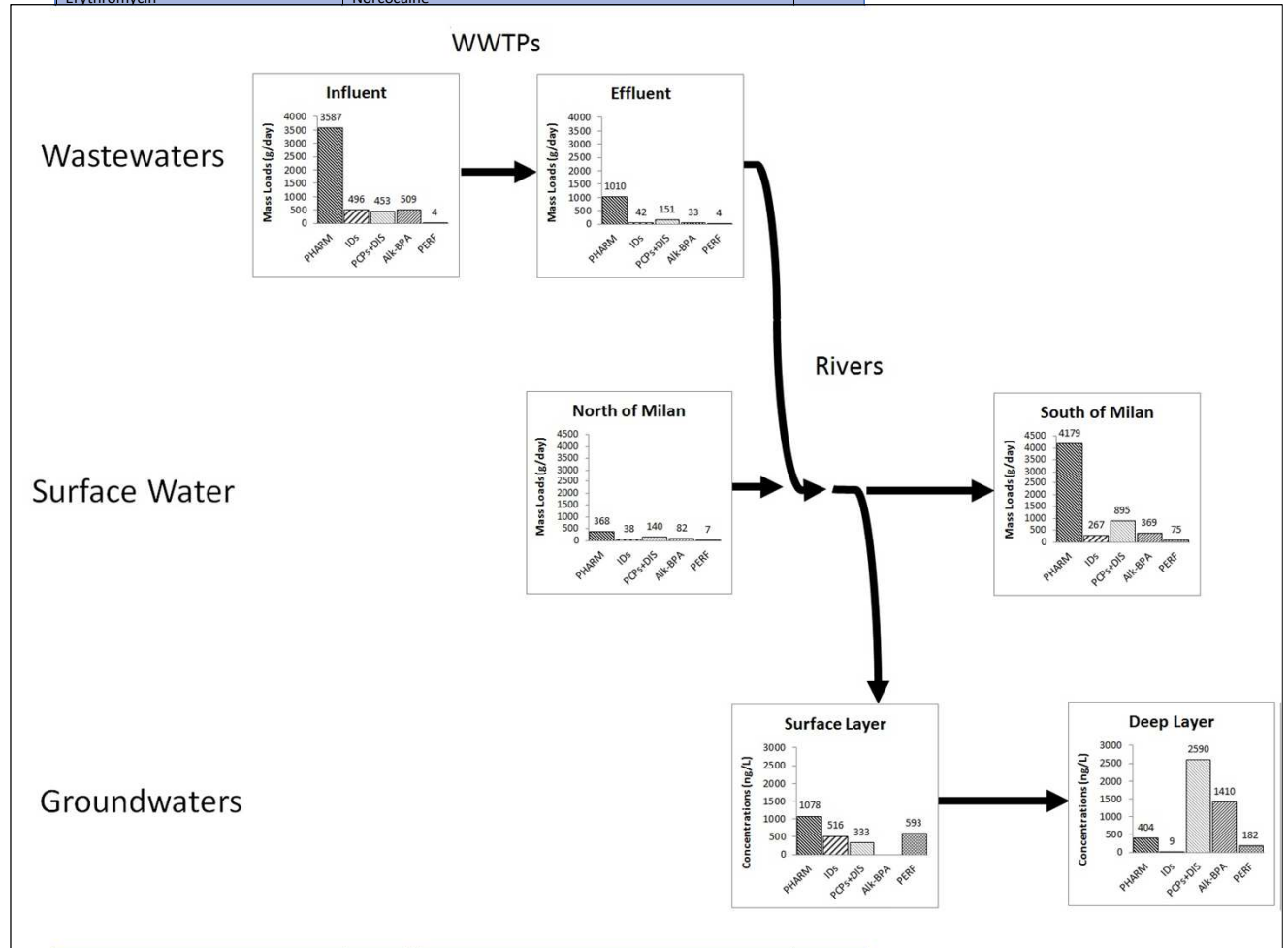
Mass balance of emerging contaminants in the water cycle of a highly urbanized and industrialized area of Italy

Sara Castiglioni <sup>a,\*</sup>, Enrico Davoli <sup>a</sup>, Francesco Riva <sup>a</sup>, Marinella Palmiotto <sup>a</sup>, Paolo Camporini <sup>a</sup>, Angela Manenti <sup>b</sup>, Ettore Zuccato <sup>a</sup>

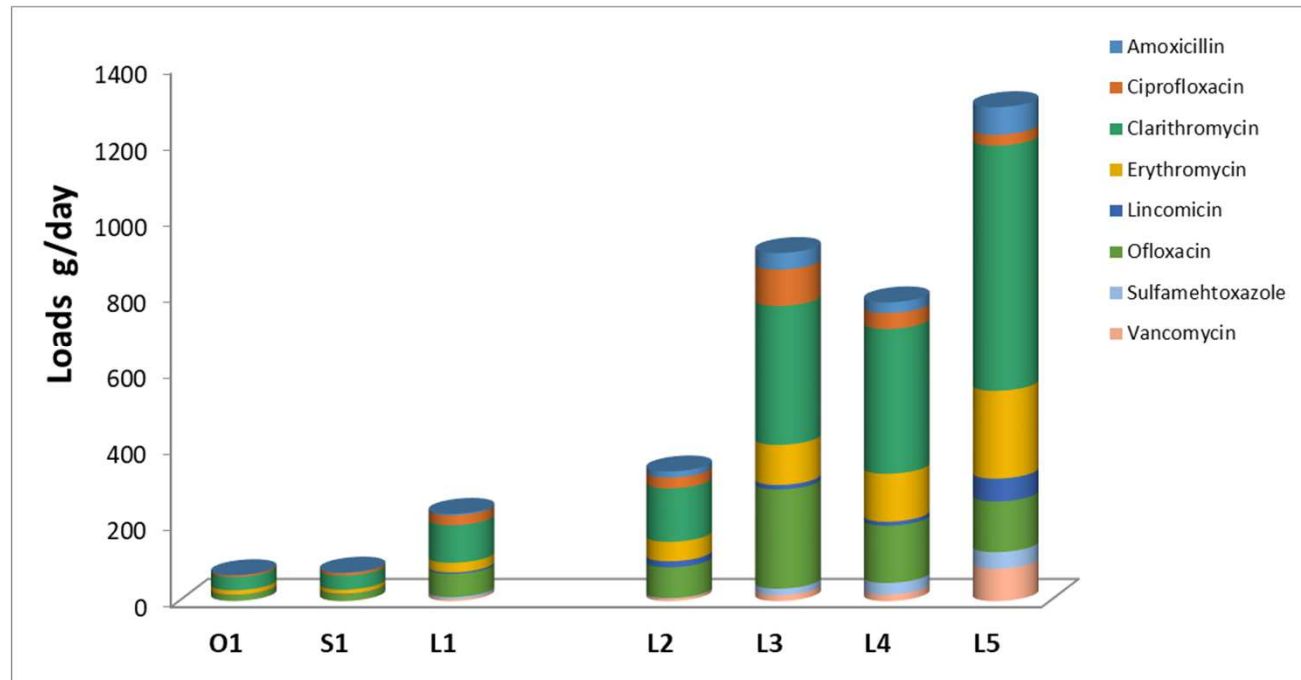
<sup>a</sup> IRCCS – Istituto di Ricerche Farmacologiche “Mario Negri”, Department of Environmental Health Sciences, Via La Masa 19, 20156 Milan, Italy  
<sup>b</sup> Metropolitana Milanese S.p.A., Area Acquedotto, Via Giuseppe Meda 44, 20141 Milan, Italy



Emerging Contaminants Investigated – MARIO NEGRI	
PHARMACEUTICALS	ILICIT DRUGS
<b>Antibiotics</b>	<b>Cocaine and metabolites</b>
Amoxicillin	Benzoylcegonine
Ciprofloxacin	Norbenzoylcegonine
Clarithromycin	Cocaine
Erythromycin	Norcocaine



# Antibiotics in Surface Water (Lambro, Seveso, Olona)

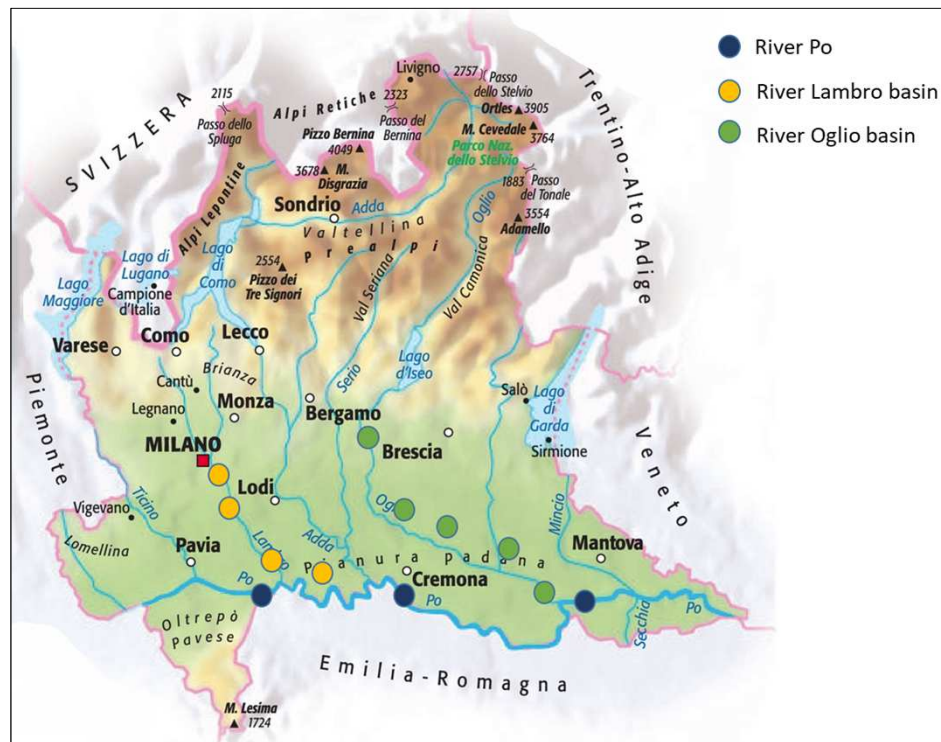


In: Gli antibiotici spiegati bene – Silvio Garattini- Edizioni LSWR, 2020

# Assessing antibiotics burden in surface water

Monitoring the **presence of antibiotics for human and veterinary use** and other pharmaceuticals in surface water in the North of Italy

## Study area



## Sampling period

Three sampling campaigns

1. Autumn – winter 2020- 2021
2. Spring 2021
3. Summer 2021

# Assessing antibiotics burden in surface water

## Selected Analytes

**Antibiotics** were selected among the most used in veterinary medicine (with some for human use)

**Other pharmaceuticals** were selected among the most used in human medicine

Antibiotics		Other Pharmaceuticals
<b><i>Sulfonamides</i></b>	<b><i>Fluoroquinolones</i></b>	<b><i>CNS drugs</i></b>
sulfamethoxazole	ciprofloxacin	diazepam
sulfadiazina	flumequine	demethyl-diazepam
sulfadimetossina	levofloxacin	<i>carbamazepine</i>
<b><i>Penicillins</i></b>	<b><i>Amphenicols</i></b>	<b><i>Diuretics</i></b>
amoxicillin	florfenicol	furosemide
ampicillin	thiamphenicol	hydrochlorothiazide
benzylpenicillin	<b><i>Diaminopiridine</i></b>	<b><i>Bronchodilators</i></b>
<b><i>Macrolides</i></b>	trimetoprim	salbutamol
spiramycin	<b><i>Tetraciclins</i></b>	<b><i>Anti-inflammatorys</i></b>
tylosin	doxycycline	ibuprofen
tilmicosin	chlortetracycline	naproxene
oleandomicin	oxytetracycline	ketoprofen
erythromycin	<b><i>Anthelmintics</i></b>	diclofenac
<b><i>Lincosamides</i></b>	ivermectine	
lincomycin	levamisol	

# Method of analysis for pharmaceuticals

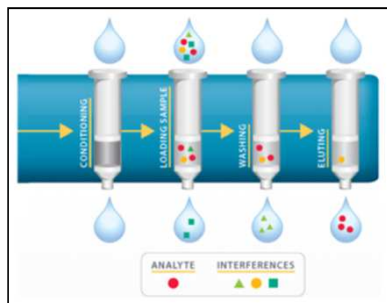


## Sample preparation

Filtration on 1.6 and 0.45  $\mu\text{m}$  filters

## Sample extraction

Cartridges Oasis MCX ed HLB (60 mg)  
Two different protocols



## Sample analysis

HPLC- MS/MS  
(API 5500 QqQ)

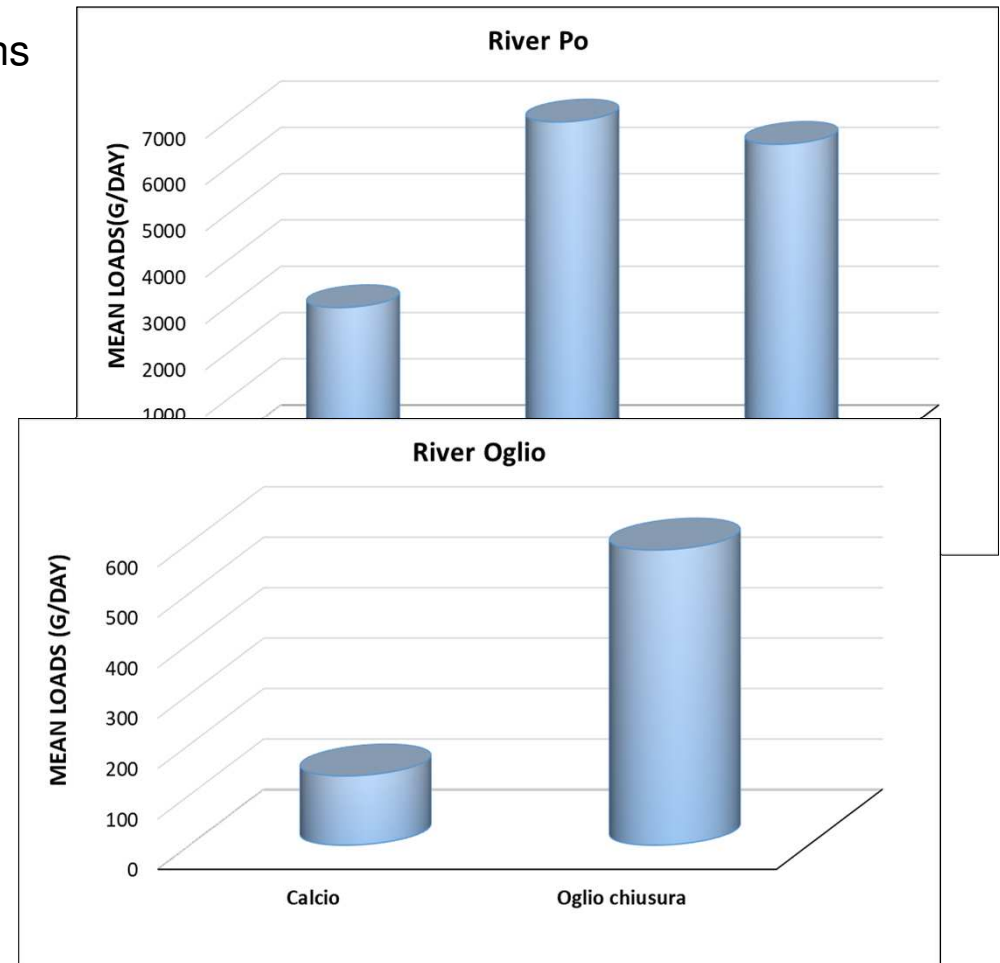
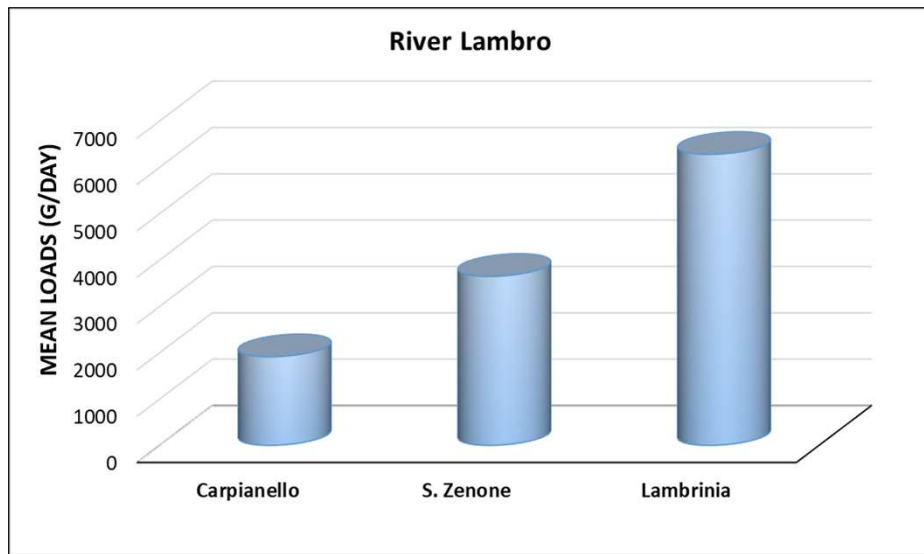


- Multiple reaction Monitoring (MRM)
- Two/three most abundant fragmentation products of the protonated pseudo-molecular ions
- Positive and negative ionization mode



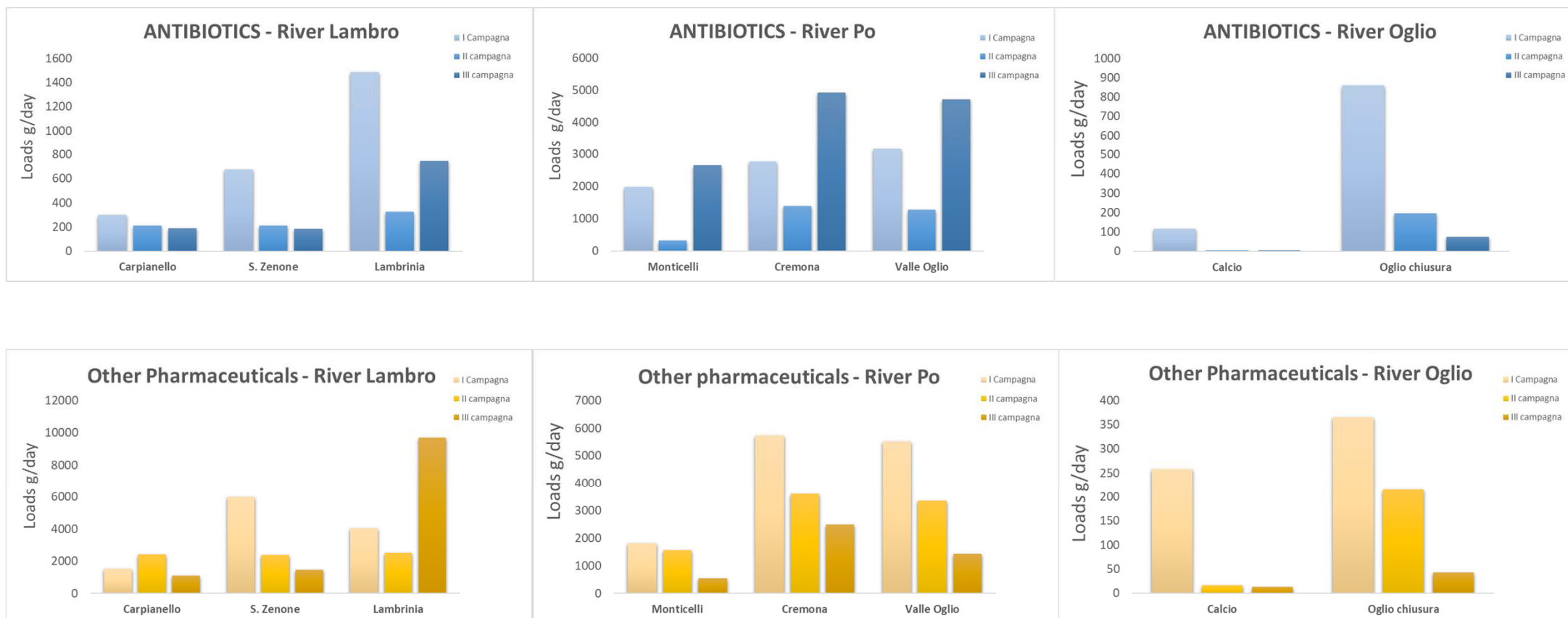
# Pharmaceuticals in surface water – Overall Results

Mean Mass Loads (g/day) from three analytical campaigns



# Pharmaceuticals in surface water – Seasonal variability

First campaign: autumn – winter; second campaign: spring; third campaign: summer



## Conclusions and future investigations

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**Increasing** burden of pharmaceuticals along the investigated rivers

Quantitative Assessment of **most abundant substances** along the rivers

**Local contamination** of specific substances in some sampling sites

Identification of **potential sources of contamination** for specific substances

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# THANKS FOR ATTENTION !!

## **Istituto Mario Negri**

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