Sara Castiglioni
Mario Negri Institute
Department of Environmental Health Sciences

Quadro della presenza dei farmaci nel ciclo idrico di Milano e Provincia

Sara Castiglioni, Ettore Zuccato

MICROINQUINANTI E CONTAMINANTI EMERGENTI,
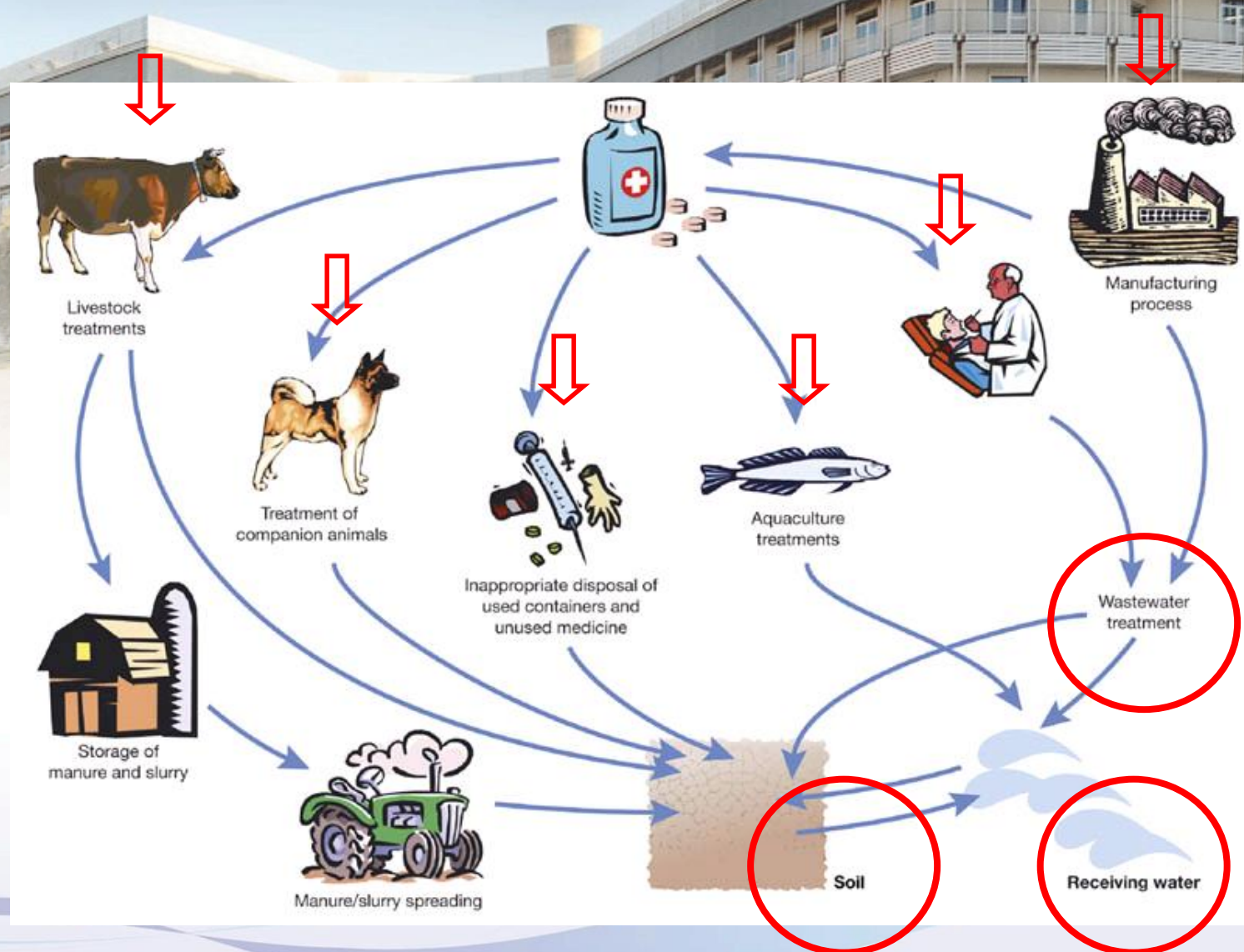Politecnico di Milano, 11-12 Giugno 2018

DEPARTMENT
Environmental
Health Sciences

Pharmaceuticals in the environment

✓ Used in **high quantities**

✓ **Heterogeneous group**

✓ Continuos **discharge**

✓ **Polar compounds** (generally small)

✓ Biologically **active substances**

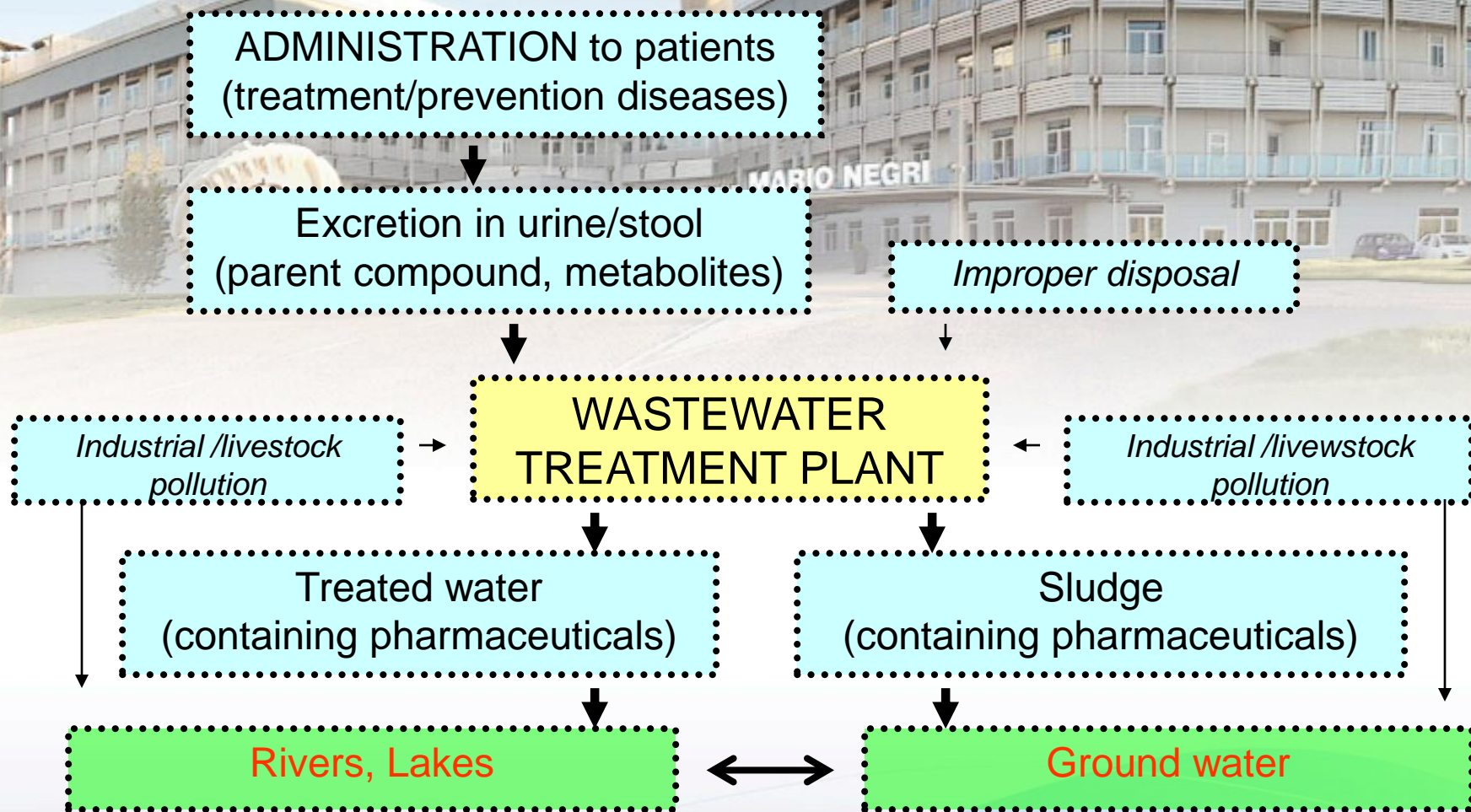✓ Complex **mixtures** – potential **toxic effects**

✓ Not **regulated**

Where pharmaceuticals comes from?

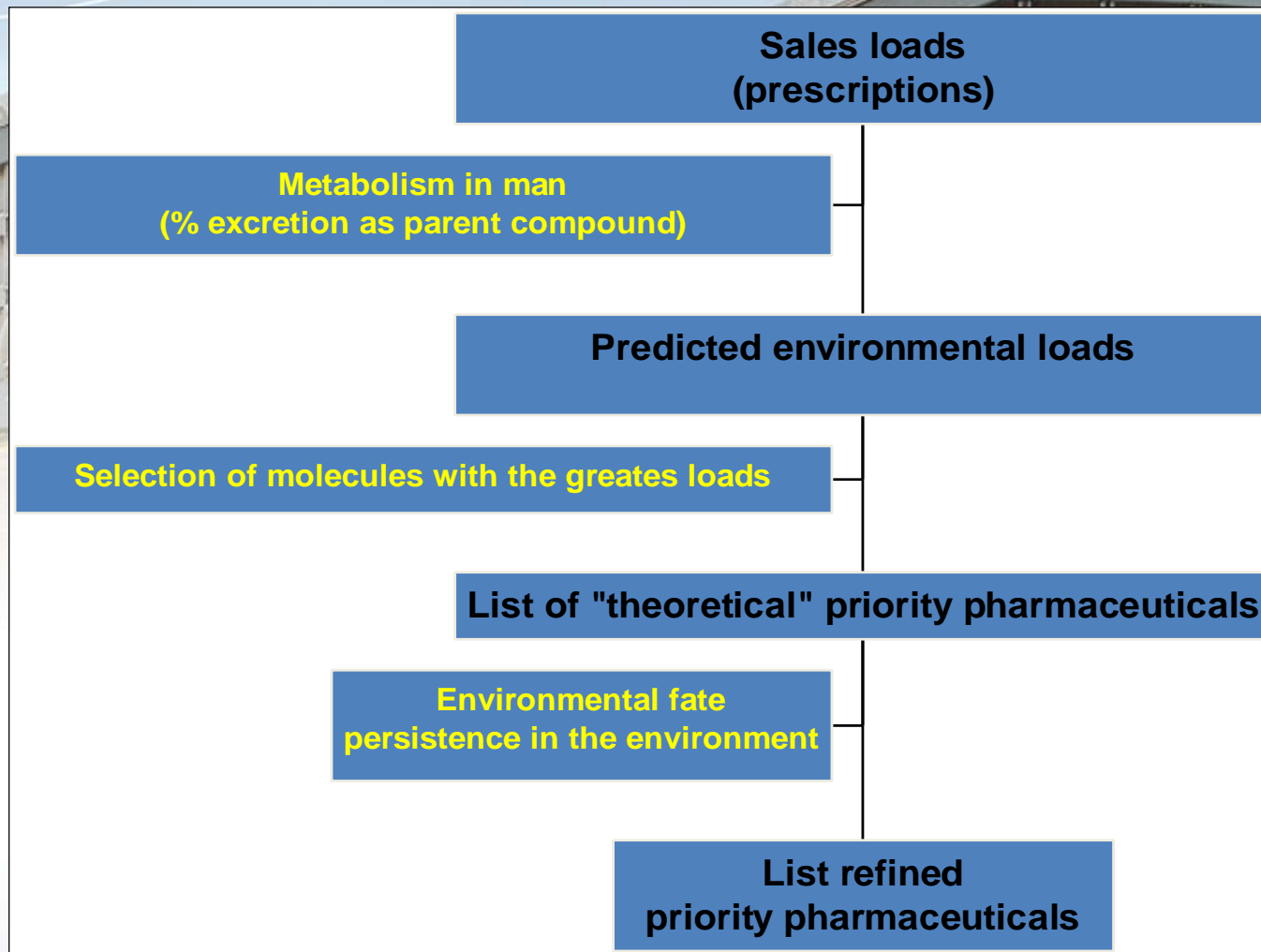**Main sources:** therapeutic treatment in human and veterinary medicine

Environmental contamination pathways

Fate and behaviour in a wastewater treatment plant

ADMINISTRATION to patients
(treatment/prevention diseases)

Excretion in urine/stool
(parent compound, metabolites)

Improper disposal

Industrial /livestock pollution

WASTEWATER TREATMENT PLANT

Industrial /livewstock pollution

Treated water
(containing pharmaceuticals)

Sludge
(containing pharmaceuticals)

Rivers, Lakes

Ground water

Pharmaceuticals Prioritisation

Sales loads (prescriptions)

Metabolism in man (% excretion as parent compound)

Predicted environmental loads

Selection of molecules with the greates loads

List of "theoretical" priority pharmaceuticals

Environmental fate persistence in the environment

List refined priority pharmaceuticals

(Zuccato et al. Lancet 2000; Calamari et al. ES&T 2003)

Pharmaceuticals Prioritisation

Table 4

Predicted environmental loads of the pharmaceuticals (priority list).

Pharmaceutical (active substance – a.s.)	Prescriptions (tons/year of a.s.)	Excretion rate in man (%)	Predicted environmental load (tons/year of a.s.)
Acetaminophen	157	54.5	85.5
Amoxicillin	156	60.0	93.8
Atenolol	17.6	82.5	14.5
Atorvastatin	10.2	2	0.2
Ciprofloxacin	21.9	40	8.8
Clarithromycin	28.5	25	7.1
Diclofenac	3.6	61	2.2
Enalapril	2.9	19.5	0.6
Furosemide	20	78.5	15.7
Hydrochlorothiazide	10.7	95	10.1
Ibuprofen	21.6	12.5	2.7
Irbesartan	31.2	3	0.9
Ketoprofen	0.7	73.5	0.5
Lansoprazole	14.2	2	0.3
Levofloxacin	17.5	78	13.7
Losartan	8.3	4.5	0.37
Metformin	819	79	647
Naproxen	2.9	70	2.03
Paroxetine	3.3	2	0.07
Ramipril	3.5	5	0.18
Rosuvastatin	3.5	5	0.17
Simvastatin	10.2	11	1.13
Valsartan	43.6	87	37.9

Riva et al., *Journal of Pharmaceutical and Biomedical Analysis*, 2015

Pharmaceuticals occurrence in the environment

Presence of therapeutic drugs in the environment

Ettore Zuccato, Davide Calamari, Marco Natangelo, Roberto Fanelli

The Lancet, 2000, 355, 1789-1790

First monitoring study of **pharmaceuticals** in surface, drinking water and river sediments in Italy

Drug	Drinking water (ng/L)			River water (ng/L)			LOD (ng/L)	River sediments (ng/kg)			LOD (ng/kg)
	Mi	Lodi*	Va	Lambro (Mi)*	Po (Pc, Cr)*	Adda (So)		Lambro (Mi)	Po (Pc, Cr)*	Adda (So)	
Atenolol	nd	nd	nd	169·9–241·9	49·5–84·3	nd	0·05	nd	nd	nd	24
Bezafibrate	nd	nd	nd	134·3–202·7	15·1–22·4	1·6	0·05	130	nd	nd	25
Ceftriaxone	nd	nd	nd	nd	nd	nd	1·80	nd	nd	nd	88
Clofibric acid	nd	3·2–5·3	nd	nd	nd	nd	1·50	nd	nd	nd	260
Cyclophosphamide	nd	nd	nd	2·2–10·1	nd	nd	0·02	nd	nd	nd	12
Diazepam	nd	19·6–23·5	0·2	0·7–1·2	0·5–0·7	nd	0·02	nd	nd	nd	9
Erythromycin	nd	nd	nd	nd–17·4	0·7–0·9	nd	0·03	630	400–600	10	1·2
Furosemide	nd	nd	nd	85·1–88	nd	nd	4·30	nd	nd	nd	210
Ibuprofen	nd	nd	nd	90·6–92·4	nd–4·0	1·0	0·50	220	nd	nd	40
Lincomycin	nd	nd	nd	6·8–13·8	1·2–4·6	nd	0·02	130	nd	nd	0·8
Oleandomycin	nd	nd	nd	nd–0·8	0·4–4·8	2·7	0·02	nd	nd	nd	11
Ranitidine	nd	nd	nd	nd–9·4	nd	nd	0·01	150	nd–410	nd	7
Salbutamol	nd	nd	nd	nd–3·1	nd–4·6	nd	0·02	nd	nd	nd	10
Spiramycin	nd	nd	nd	8·4–68·3	nd	nd	0·75	2900	nd–380	380	375
Tilmicosin	nd	nd	nd	nd	nd	nd	0·75	nd	nd	nd	375
Tylosin	nd	0·6–1·7	nd	nd–2·2	nd	nd	0·25	2640	nd–130	nd	125

Mi=Milan, Va=Varese, Pc=Piacenza, Cr=Cremona, So=Sondrio. Amoxycillin and ceftazidime excluded because analytical methods not sensitive enough.
*Two sampling sites.

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI IRCCS

Pharmaceuticals occurrence in the environment

Removal of Pharmaceuticals in Sewage Treatment Plants in Italy

SARA CASTIGLIONI,[†,‡] RENZO BAGNATI,[‡]
ROBERTO FANELLI,[‡]
FRANCESCO POMATI,[†]
DAVIDE CALAMARI,[†] AND
ETTORE ZUCCATO*,[‡]

TABLE 6. Summary of Loads and Removal Rates (RR) in STPs and Attenuation Rates and Residual Loads in Surface Water for the Most Abundant Pharmaceuticals

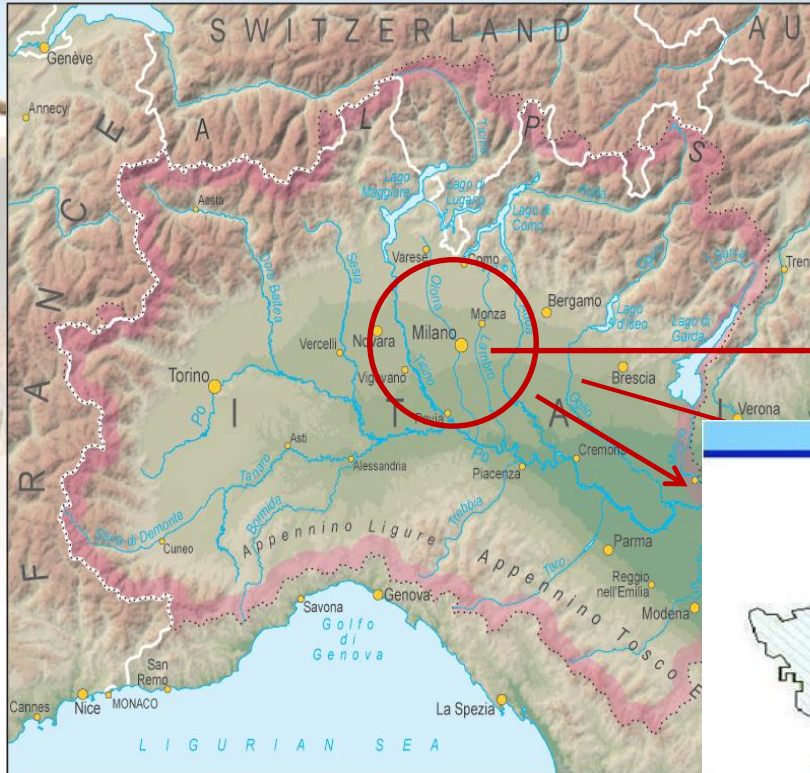| pharmaceutical	load in influent (mg/day/1000 inh)[a]	RR in STP (%)[a]	residual load in effluent (mg/day/1000 inh)[a]	attenuation in river (%)[a]	residual load in surface water (mg/day/1000 inh)[a]	occurrence in particulate (+/−)
atenolol	494	21	281	28	257	+
ofloxacin	360	57	233	27	94	+
hydrochlorothiazide	354	44	415	64	197	+
furosemide	277	15	195	27	66	−
ciprofloxacin	259	63	97	5	224	+
ranitidine	188	72	96	17	33	+
ibuprofen	122	55	28	21	35	−
sulfamethoxazole	65	24	10	3	122	−
bezafibrate	50	30	29	34	38	+
enalapril	31	69	1.2	22	6	+
clarithromycin	21	0	55	41	66	+
carbamazepine	12	0	28	22	28	+
erythromycin	5	0	5	35	3	+
spiramycin	5	0	35	46	30	+
salbutamol	4	0	4	27	2	−
lincomycin	3	0	5	18	4	−

[a] Median values.

Aim of the study

Evaluate presence and distribution of selected emerging contaminants in the aquatic environment in the area of Milan
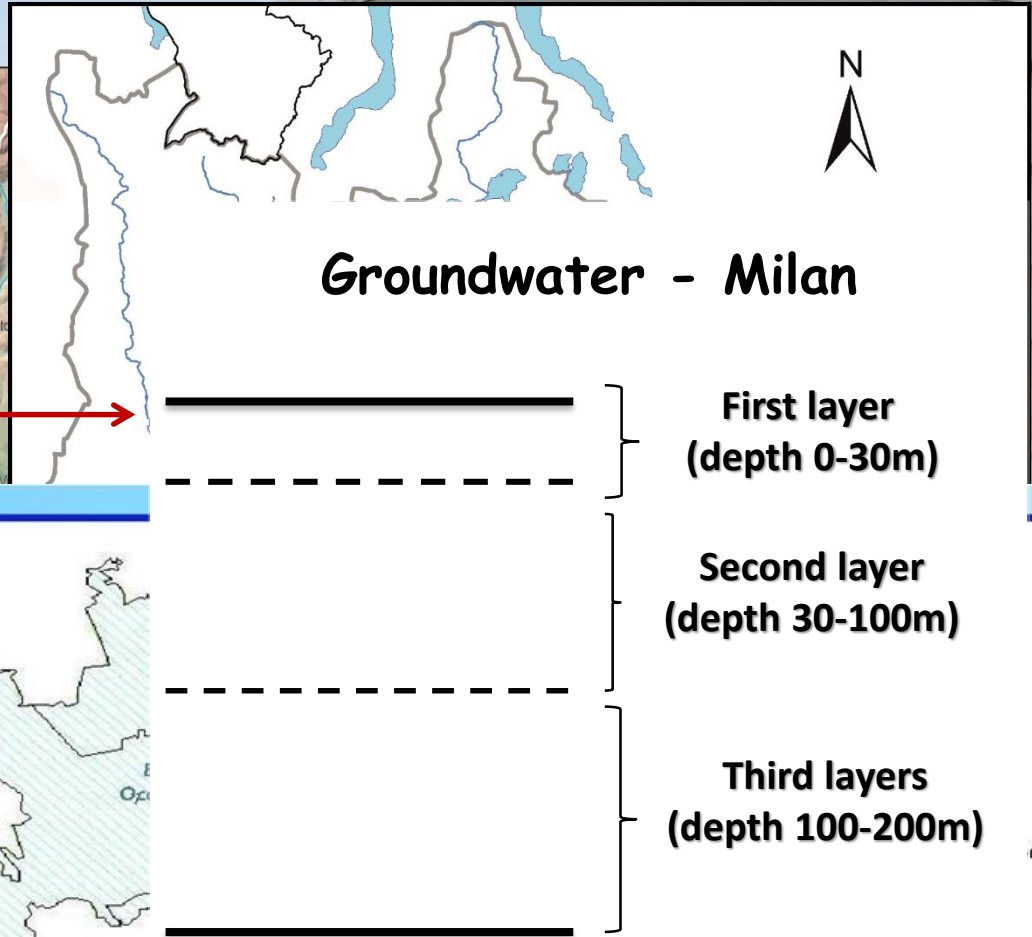
➢ Selection of **environmental pollutants**

➢ Set up of **analytical methods**

➢ **Monitoring occurrence** and **fate** in:

  ✓ wastewater (raw and treated)

  ✓ surface water

  ✓ groundwater

➢ **Mass balance of pollutants** in the River Lambro basin

➢Environmental and Human **Risk Assessment**

Sampling sites

North of Italy, Milan Area

Groundwater - Milan

First layer (depth 0-30m)

Second layer (depth 30-100m)

Third layers (depth 100-200m)

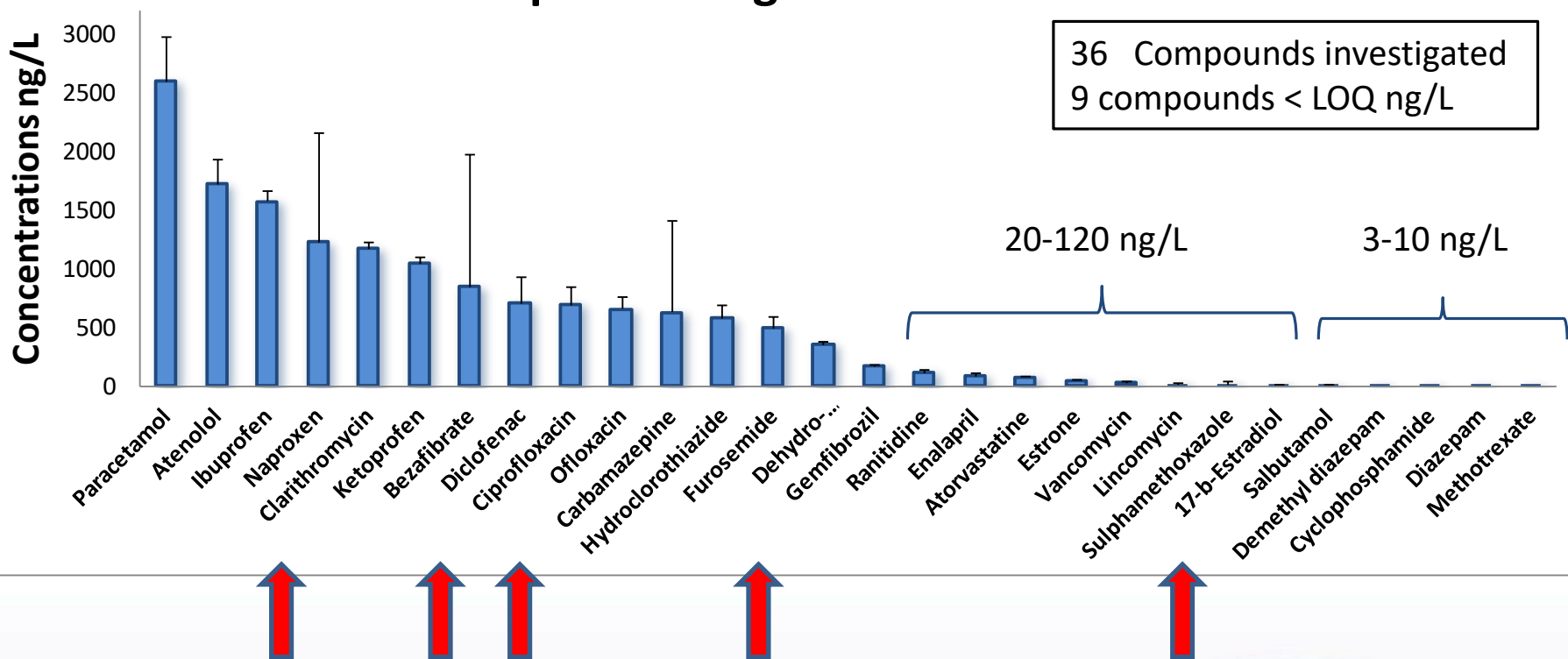Impianto di Depurazione di Milano Nosedo

Impianto di Depurazione di Milano San Rocco

Pharmaceuticals in Untreated Wastewater

Three plants, 7 days sampling for each plant, March 2011

Therapeutic drugs -Raw Wastewater

36 Compounds investigated
9 compounds < LOQ ng/L

20-120 ng/L

3-10 ng/L

Concentrations ng/L

Paracetamol, Atenolol, Ibuprofen, Naproxen, Clarithromycin, Ketoprofen, Bezafibrate, Diclofenac, Ciprofloxacin, Ofloxacin, Carbamazepine, Hydroclorothiazide, Furosemide, Dehydro-..., Gemfibrozil, Ranitidine, Enalapril, Atorvastatine, Estrone, Vancomycin, Lincomycin, Sulphamethoxazole, 17-b-Estradiol, Salbutamol, Demethyl diazepam, Cyclophosphamide, Diazepam, Methotrexate
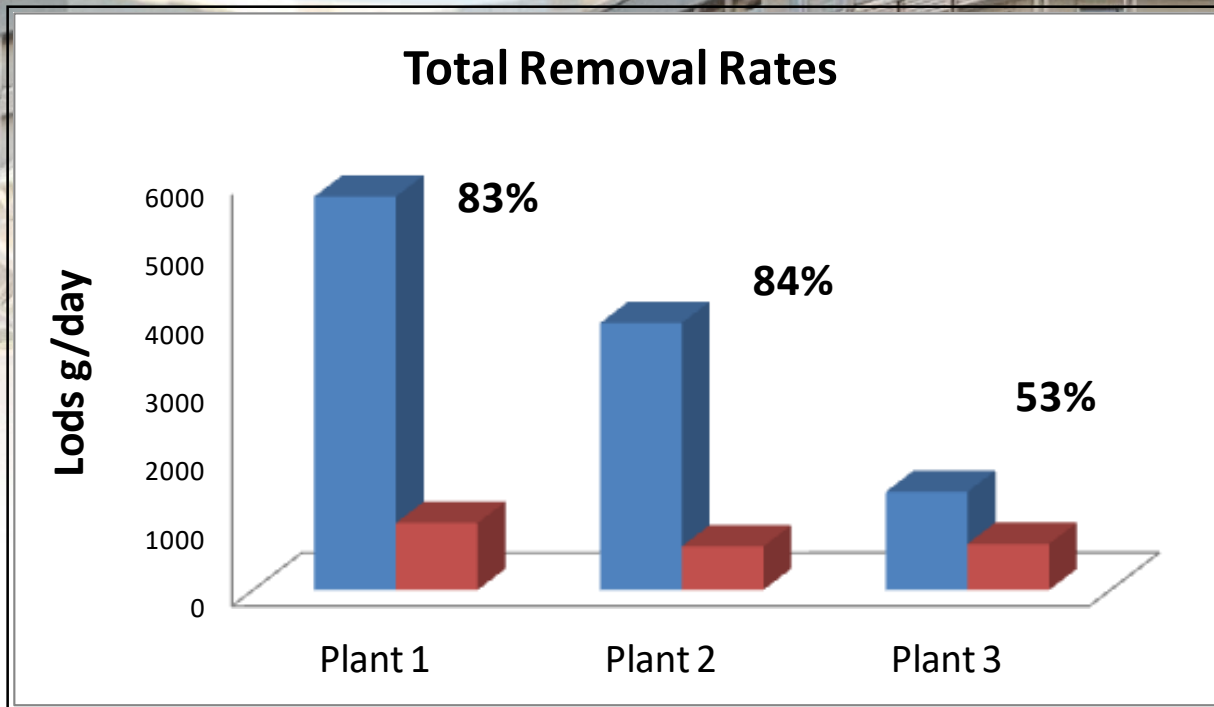
Castiglioni et al. *Water Research* 2018

Removal of pharmaceuticals in WWTPs

Therapeutic drugs: different removals among STPs

Total Removal Rates

(Chart: Lods g/day vs Plant 1, Plant 2, Plant 3. Plant 1: 83%, Plant 2: 84%, Plant 3: 53%)

Plant 1 and 2: Activated sludge secondary treatment followed by disinfection

Plant 3: Biofilters secondary treatment and UV disinfection

Castiglioni et al. *Water Research* 2018

Removal of emerging contaminants in WWTPs

Removals depends on compounds and treatment

Plant 1 and 2: Activated sludge secondary treatment followed by disinfection

Plant 3: Biofilters secondary treatment and UV disinfection

| Selected Pharmaceuticals	Influent PLANT 1 (7 samples) (g/d)	Effluent PLANT 1 (7 samples) (g/d)	Influent PLANT 2 (7 samples) (g/d)	Effluent PLANT 2 (7 samples) (g/d)	Influent PLANT 3 (7 samples) (g/d)	Effluent PLANT 3 (7 samples) (g/d)	Removal rate (%) PLANT 1	PLANT 2	PLANT 3
Atenolol	731±189	100±15	593±53	161±45	132±18	108±105	86	73	18
Bezafibrate	66±42	5±2	36±8	50±22	226±208	132±105	92	0	42
Carbamazepine	138±40	73±12	104±13	88±8	133±143	23±3	47	15	83
Ciprofloxacin	172±47	35±9	229±35	51±16	53±34	30±8	80	78	43
Clarithromycin	445±90	73±14	152±29	92±11	89±16	81±10	84	39	9
Furosemide	326±148	117±32	115±49	528±57	55±22	49±3	64	0	11
Ibuprofen	668±192	1.2±0.1	485±106	7±5.2	87±18	17±6	100	99	80
Hydrochlorothiazide	323±127	417±403	139±19	289±28	38±7	13±9	0	0	66
Ketoprofene	621±296	76.4±26	265±17	152±61	86±21	17±10	88	42	80
Naproxene	612±224	23±5	286±140	55±69	57±9	51±6	96	81	11
Ofloxacin	106±28	50±8	191±28	78±6	47±29	39±11	53	59	17
Ranitidine	36±11	1.3±0.3	45±13	31±3	11±3	15±3	96	31	0

Castiglioni et al. *Water Research* 2018

Pharmaceuticals in Surface Water

Castiglioni et al. *Water Research* 2018

Pharmaceuticals in Surface Water

Rivers
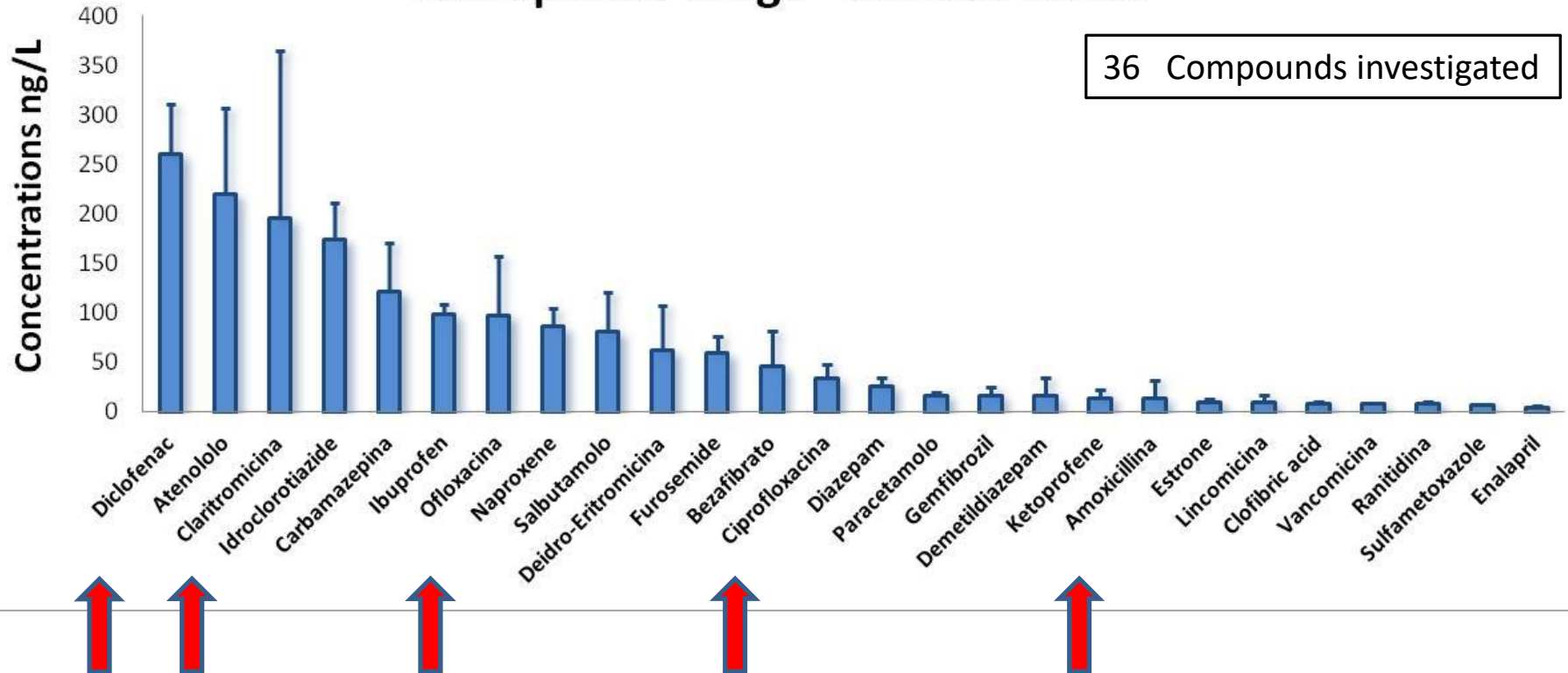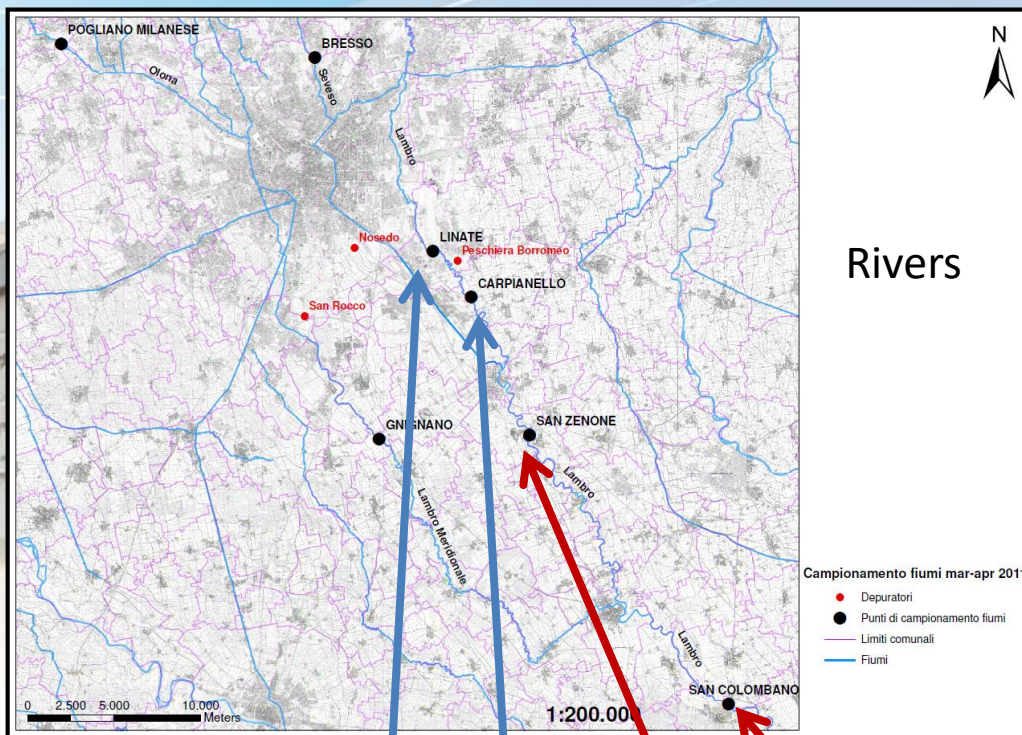
Suspected source: Use in **livestock** holdings

Concentrations	Lambro			
ng/L	Linate	Carpianello	San Zenone	San Colombano
Atenolol	252	291	264	224
Carbamazepine	71	131	98	119
Clarythromicin	202	323	305	261
Diazepam	0.3	0.8	84	52
Demetil-Diazepam	0.9	1.4	122	72
Salbutamol	1.9	2.7	453	288

Castiglioni et al. *Water Research* 2018

Pharmaceuticals in Surface Water

Mass Loads are calculated considering the mean concentrations of two analytical campaigns (March - September)
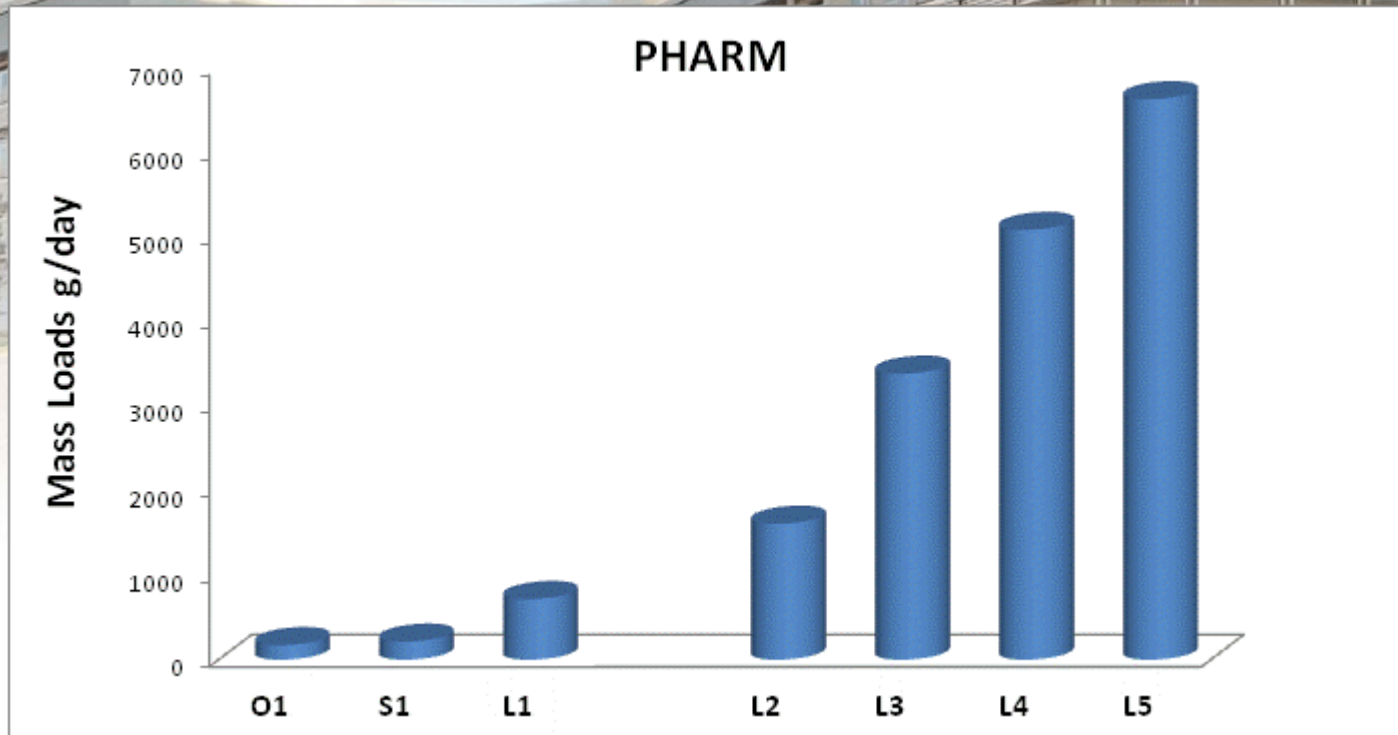
Mass Loads increase in the river Lambro basin

Castiglioni et al. *Water Research* 2018

Mass balance of emerging contaminants

Mass Balance of the Emerging Contaminants in the Lambro River Basin

Classes of compounds	Rivers before Milan	WWTPs Effluents in Milan	Closure of the Lambro River basin	Sources in the south of Milan
Loads (g/day)				
Therapeutic Drugs	1105	3009	6634	2520
All ECs	6822	3872	22967	12273

Castiglioni et al. *Water Research* 2018
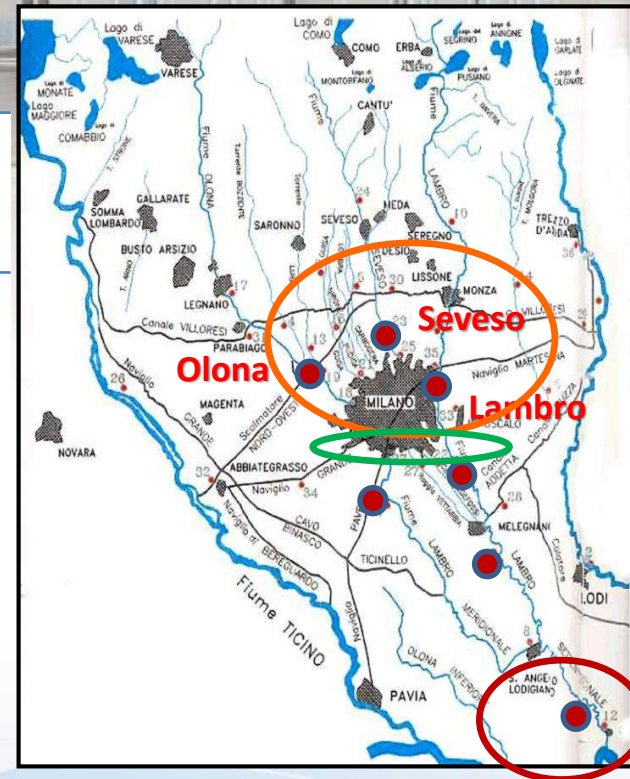
Ground Water Contamination

Table 3

ECs in groundwater from the surface and deeper layers in the city of Milan. Concentrations are in ng/L.

| Surface Layer (32 samples)	Frequency of detection	Median	Range	Deep Layers (21 samples)	Frequency of detection	Median	Range
PHARM				**PHARM**			
Atenolol	2 (32)	1.6	0.6–2.5	Atenolol	4 (21)	0.5	0.5–3.0
Diazepam	4 (32)	1.5	0.6–2.9	Diazepam	3 (21)	0.2	0.3–1.0
Carbamazepine	32 (32)	20.0	1.5–152	Carbamazepine	21 (21)	14.5	0.2–32
Lincomycin	1 (32)	0.4	–	Lincomycin	2 (21)	0.6	0.4–0.9
Bezafibrate	1 (32)	0.8	–	Bezafibrate	1 (21)	0.3	
Hydrochlorothiazide	5 (32)	1.1	0.9–14	Clofibric acid	10 (21)	0.3	0.14–2.3
Sulfamethoxazole	10 (32)	0.9	0.7–16	DehydroErythromycin	7 (21)	9.6	3.7–13.2
Ibuprofen	4 (32)	1.1	0.6–14.2	Clarithromycin	6 (21)	7.4	4.7–10.4
IDs				**IDs**			
Benzoylecgonine	23 (32)	0.8	0.4–4.1	Benzoylecgonine	18 (21)	0.3	0.2–0.7
Norbenzoylecgonine	3 (32)	0.8	0.6–1.0	Norbenzoylecgonine	13 (21)	0.2	0.13–0.3
Cocaine	10 (32)	0.8	0.5–2.7	**PCPs**			
Hydrocodone	1 (32)	13.0	–	PBSA	5 (21)	10.9	3.7–1853
Oxycodone	6 (32)	22.2	7.2–286	**PERF**			
PCPs				PFOS	19 (21)	2.4	1.2–9.0
PBSA	2 (32)	45.4	44–46	PFOA	21 (21)	5.6	1.3–11.4
DIS				**Alk-BPA**			
Triclosan	4 (32)	62.50	32–85	Nonylphenol	21 (21)	63.6	45–107
PERF				**AM**			
PFOS	32 (32)	4.4	0.8–24	Caffeine	13 (21)	11.9	7.3–58
PFOA	32 (32)	10.3	3.7–36	Paraxanthine	1 (21)	17.7	
AM				Nicotine	2 (21)	42.8	28–58
Caffeine	14 (32)	148.0	84–683				
Paraxanthine	3 (32)	27.5	25–96				
Nicotine	27 (32)	518.0	51–14372				
Cotinine	19 (32)	8.2	2.7–28				

Castiglioni et al. *Water Research* 2018
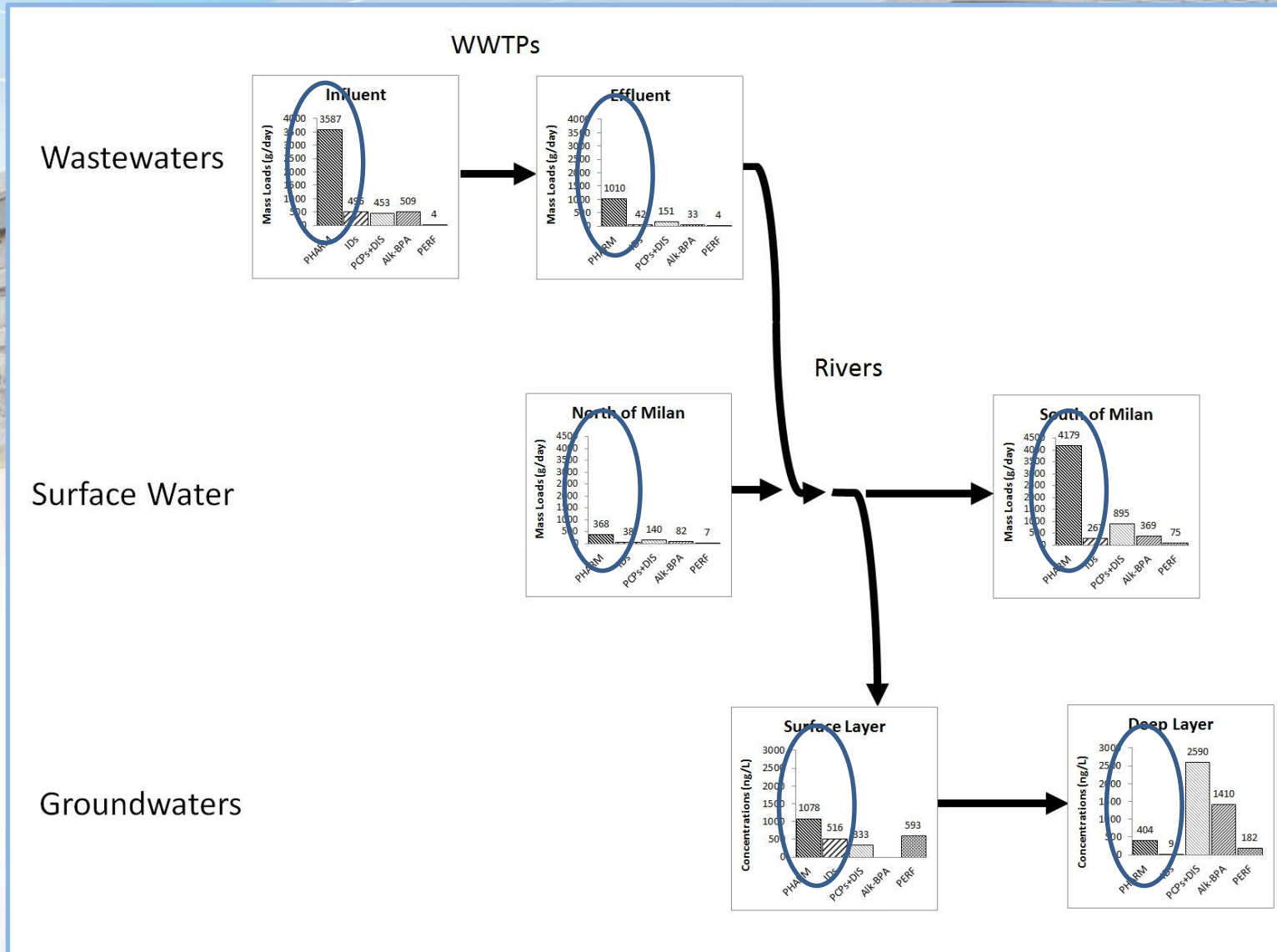
Ground Water Contamination
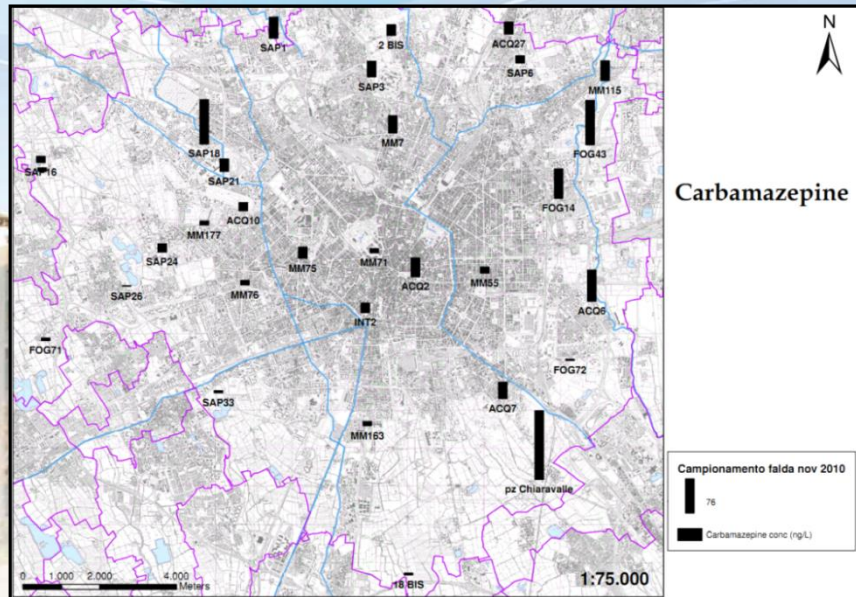
Different pattern of contamination between the layers analyzed

First layer groundwater (depth 0-30m) Concentrations 1.5-152 ng/L

Second and third layer groundwater (depth 40-200 m) Concentrations 0.2-32 ng/L
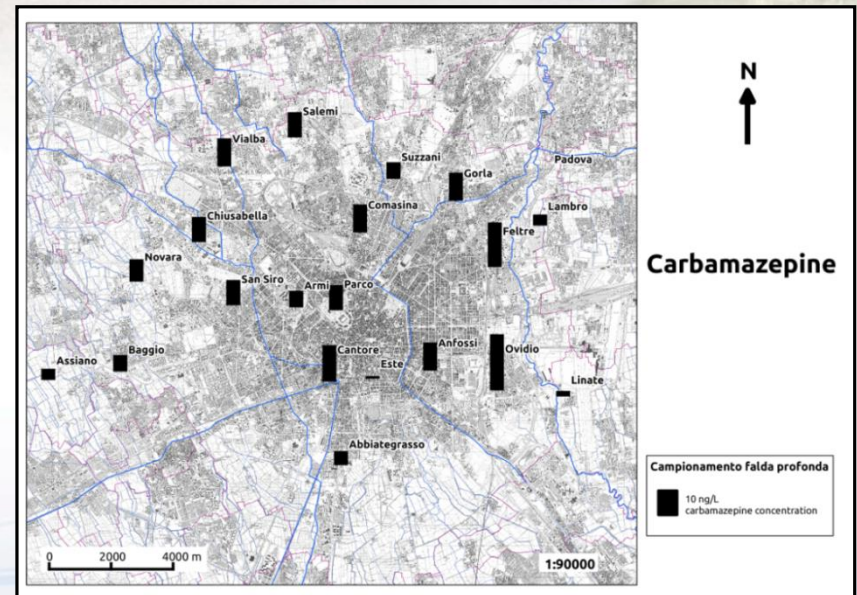
Mass balance of emerging contaminants

Conclusions

✓ Most of the **pharmaceuticals** investigated were **ubiquitous** in the River Lambro basin in a highly urbanised area

✓ **Behaviour** and **fate in WWTPs** depends on **chemicals structure** and **type of treatment** adopted

✓ **Mass Balance** calculation allowed the **identification of different sources** of contamination

- **domestic** from treated or untreated wastewater
- **livestock** in the river Lambro basin

✓ **Groundwater** resulted affected by pharmaceuticals contamination

✓ **Potential environmental risks** related to the reuse of surface water in a number of activities were identified

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Grazie per l'attenzione!

Pharmaceuticals occurrence in the environment

Journal of
Hazardous
Materials

www.elsevier.com/locate/jhazmat

Identification of the pharmaceuticals for human use contaminating the Italian aquatic environment

Ettore Zuccato [a,*], Sara Castiglioni [a,b], Roberto Fanelli [a]

Journal of Hazardous Materials 122 (2005) 205–209

Table 4
Pharmaceuticals in effluents of urban sewage treatment plants (STP) (median of nine STPs), and in surface water from the River Po (median and maximum value of seven sampling sites), and River Lambro (sampling site Milan)

ng/L	STPs	Lambro river	Po river	
	Median		Maximum	Median
Ofloxacin	600.0	306.1	37.0	33.1
Furosemide	585.0	254.7	67.2	3.5
Atenolol	466.0	241.0	41.7	17.2
Hydrochlorothiazide	439.1	255.8	24.4	4.6
Carbamazepine	291.1	175.3	34.2	23.1
Ranitidine	288.2	38.5	4	1.3
Ciprofloxacin	251.0	14.4	26.2	Nd
Sulphamethoxazole	127.2	Nd	Nd	Nd
Ibuprofen	121.2	20.0	17.4	13.0
Spiramycin	75.0	74.2	43.8	9.8
Bezafibrate	54.8	57.2	2.7	1.9
Erythromycin	47.4	4.5	15.9	3.2
Lincomycin	30.5	24.4	248.9	32.6
Clarithromycin	18.1	8.3	20.3	1.6
Salbutamol	8.7	2.5	1.7	1.1
Amoxycillin	4.7	Nd	Nd	Nd
Cyclophosphamide	0.6	Nd	Nd	Nd
Diazepam	0.0	Nd	Nd	Nd
Enalapril	0.0	0.5	0.1	0.1
Ethinylestradiol	0.0	Nd	Nd	Nd
Methotrexate	0.0	Nd	Nd	Nd
Omeprazole	0.0	Nd	Nd	Nd

Values are expressed in ng/L.

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I R C C S