Emission of pharmaceuticals from Dutch care institutions into wastewater: chemical en effect monitoring

Barry Pieters[1], Lideke Vergouwen and Stefan Kools

[1]Grontmij, Amsterdam, The Netherlands, barry.pieters@grontmij.nl

Grontmij

stowa

planning connecting respecting the future

Pharmaceuticals: emerging compounds!

Grontmij

stowa

planning connecting respecting the future

Introduction

Research on pharmaceuticals necessary?

- Not a priority compound in WFD! No environmental threshold values…
- Large diversity:

	active compounds	formulations	metabolites
Human	850	12.000	?
Veterinary	200	2.500	?

- Designed for pharmacological effect at very low concentrations
- High solubility
- Diffuse perceptions on environmental risks
- Occurrence in surface water, groundwater and drinking water

Entry routes human pharmaceuticals

Verg(h)ulde pillen project (2005-2009): HOSPITALS

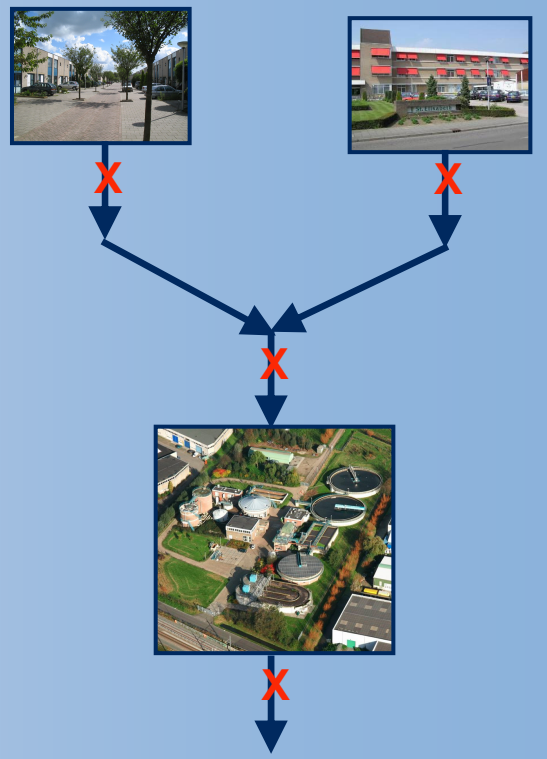
- **Description research:** Literature study and chemical monitoring of emissions from hospitals and households
- **Aim:** Characterize emissions from hospitals for recommendations on cost-effective measures for discharge reductions
- **Funding:** STOWA (Foundation for Applied Water Research)

ZORG project (2009-2010): CARE INSTITUTIONS

- **Aim:**
  - Collect data on nature and extent of pharmaceutical emissions from Dutch care institutions
  - Gather information for discussions on cost-effective measures for emission reduction
- **Set-up**
  - A. Literature study
  - B. Chemical and effect measurements in wastewater
- **Funding:** STOWA (Foundation for Applied Water Research) and participation of 8 waterboards

Set-up monitoring research

- Sample locations for monitoring
  - effluent care institutions
  - effluent households
  - influent WTP
  - effluent WTP
- Chemical analysis: 53 compounds by Omegam laboratories (LC-MS)
- Effect analysis by BDS laboratories:
  - ER-Calux assay: estrogen activity
  - GR-Calux assay: glucocorticoid activity

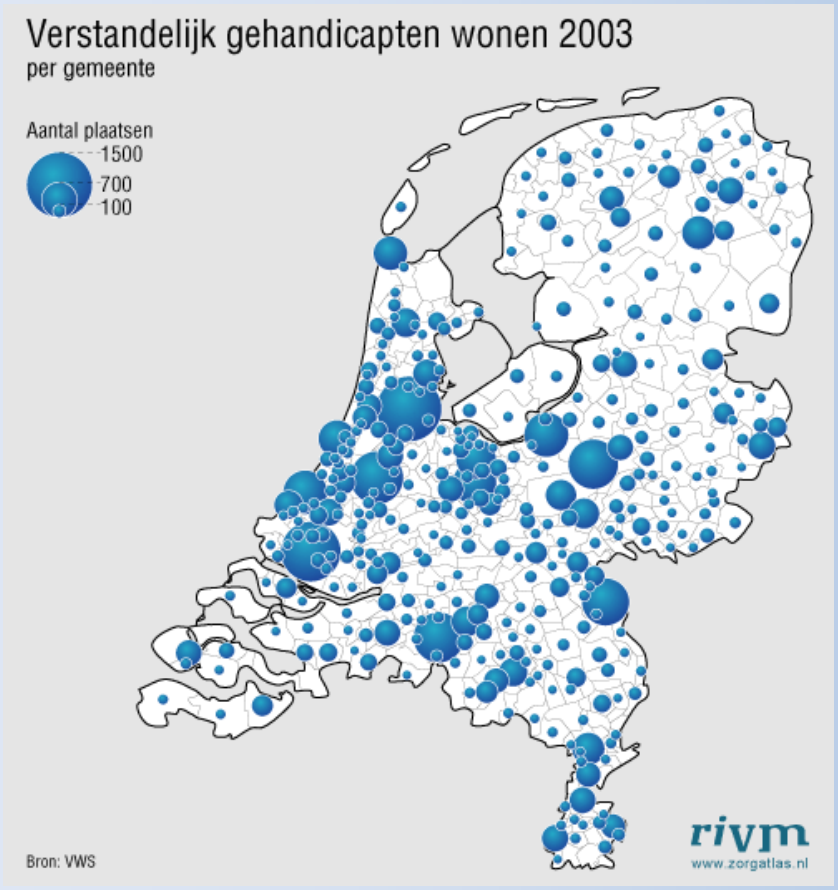


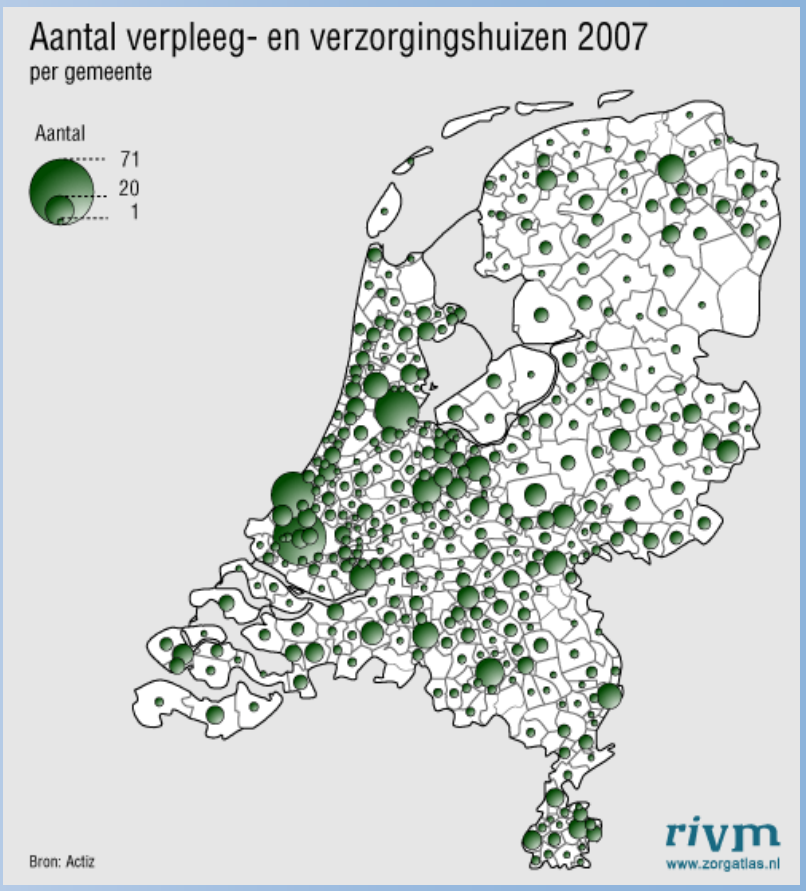
Sampling…..

A. Literature study

- **Identified types of care institutions:**
  - Home for the elderly
  - Nursery homes
  - Physical disabled
  - Mental disabled
  - Severely mental disabled (GGZ)
  - (addiction)

Nursing/elderly homes and mental disabled in The Netherlands



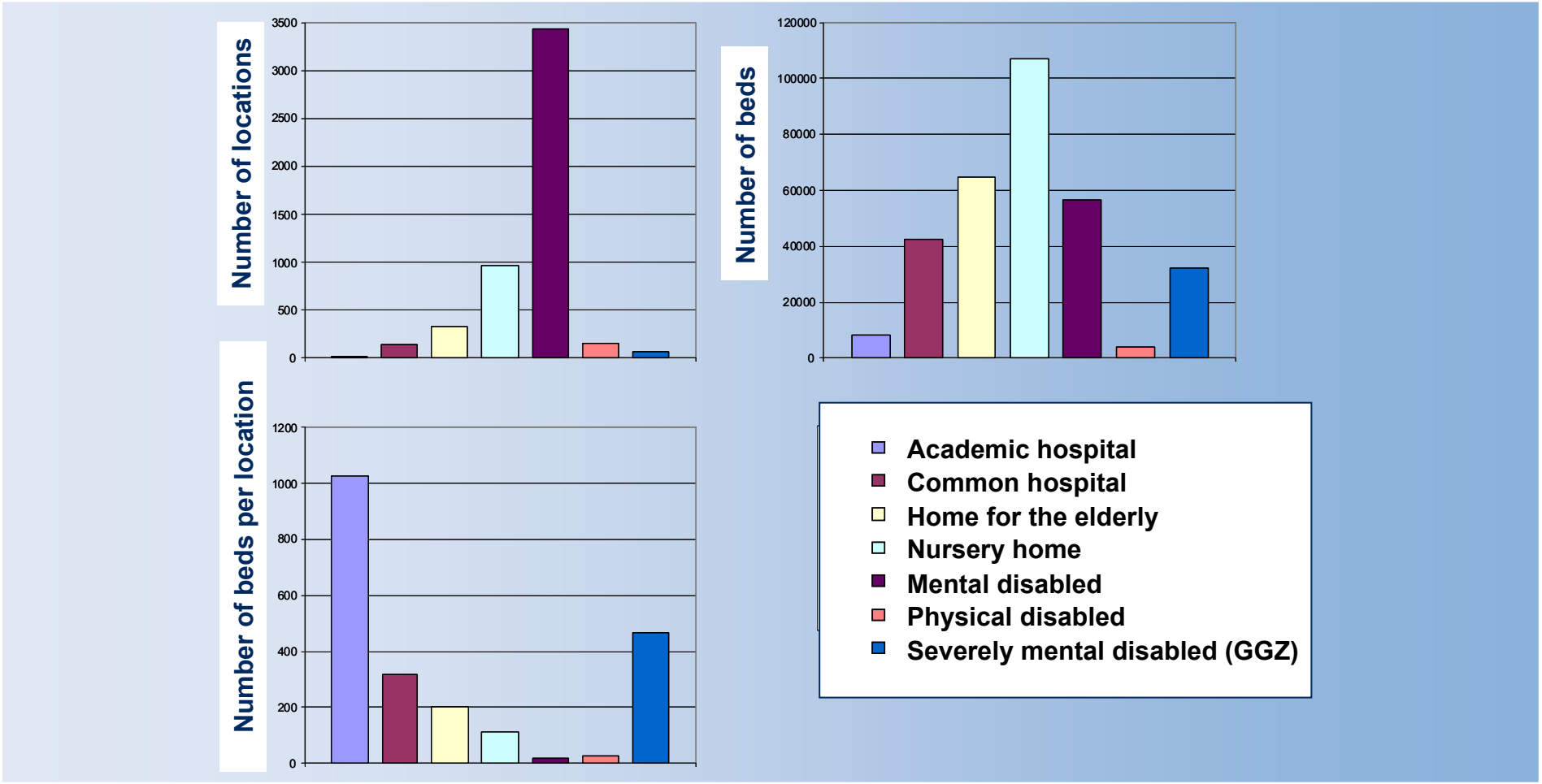


Grontmij

stowa

planning connecting
respecting
the future

Number of locations and beds per type of care institution



Determination pharmaceutical loads

- Based on inventory prescriptions
  - intake
  - calculated emission (= intake * excretion)
- Based on results chemical analysis

Aim project is to gather information which can be extrapolated to The Netherlands

Expression loads in gram/year/person

Establishment database excretion factors for 367 compounds

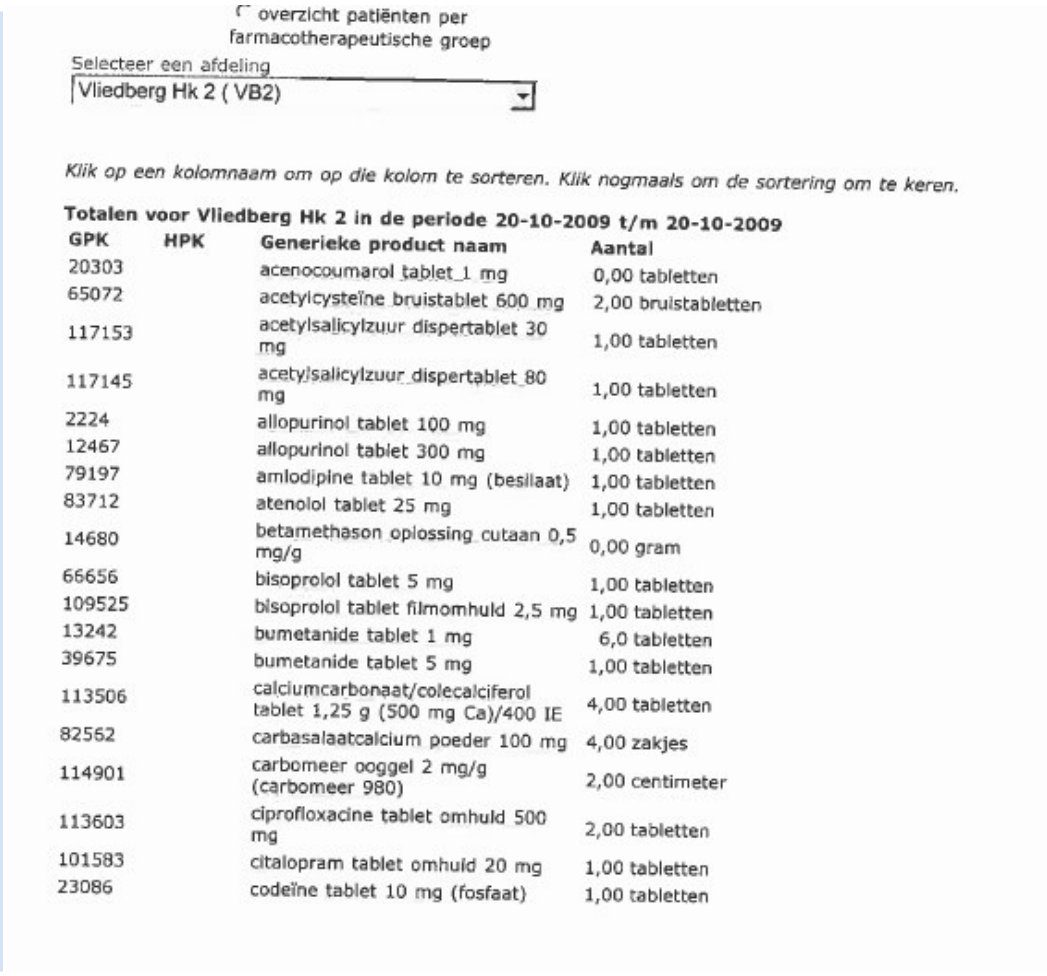
Active Compound	ATC Code	DDD range (mg) Martindale Drug Reference	DDD mean (mg)	Martindale Drug Reference	BIAM2 database	TU-Harburg database	Unchanged in urine	Unchanged in feces	Total excretion factor unchanged
Chlorhexidine	A01AB03				Mainly excreted in faeces. 15 to 25% of a dose excreted in urine.		0	0,95	0,95
Metronidazole	A01AB17	500-3000	1500	The majority of a dose of metronidazole is excreted in the urine, mainly as metabolites; a small amount appears in the faeces.	60 to 80% of a dose excreted in urine mainly as metabolites (10 to 15% as unchanged drug).	5-20	0,15	0,05	0,2
Triamcinolone	A01AC01	4-48	26	Corticosteroids are metabolised mainly in the liver but also in other tissues, and are excreted in the urine.					1
Hydrocortisone	A01AC03	20-500	260	These are excreted in the urine, mainly conjugated as glucuronides, with a very small proportion of unchanged hydrocortisone.	Mainly excreted in urine as metabolites (99%) and unchanged (1%).		0,01	0	0,01
Ranitidie	A02BA02	100-300	200	bioavailabilityabout 50%, small proportion metabolised liver, about 30% of an oral dose and 70% of an intravenous dose excreted unchanged in the urine.		30-75	0,36	0,28	0,64
Omeprazole	A02BC01	20-120	70	Almost completely metabolised in liver, metabolites are inactive and excreted mostly in the urine and to a lesser extent in bile.	77% of a dose excreted in urine as metabolites. 16 to 19% of a dose excreted in faeces.	0	0	0,19	0,19
Pantoprazole/Pantozol	A02BC02	10-40	25	Metabolites are excreted mainly (about 80%) in the urine, with the remainder being excreted in faeces via the bile.	Mainly excreted in urine as metabolites. 35% are excreted in faeces (50% as unchanged drug and 50% as metabolites).		0,05	0,2	0,25
Lansoprazol	A02BC03	15-120	67,5	Metabolites are excreted mainly in faeces via the bile; only about 15 to 30% of a dose is excreted in urine.	Mainly excreted in faeces. 15 to 25 % of a dose excreted in urine.		0,1	0,9	1
Rabeprazol	A02BC04	10-120	65	Metabolites are excreted principally in the urine (about 90%) with the remainder in the faeces.			0,9	0,1	1
Esomeprazole	A02BC05	20-160	90	Almost 80% of an oral dose is eliminated as metabolites in the urine, the remainder in the faeces.					1
Nexium (zie Esomeprazole	A02BC05								1
Mebeverine	A03AA04	150-400	275	Mebeverine is completely metabolised by hydrolysis to veratric acid and mebeverinealcohol, the latter of which may then be conjugated. The metabolites are excreted in the urine.	Excreted in urine.				1
Dimeticone/Simeticone	A03AX13	300-1000	650		Excreted as unchanged drug in faeces.	0			1
Scopolaminebutyl/Hyoscine Butylbromide	A03BB01	20-100	60	It is almost entirely metabolised, probably in the liver; only a small proportion of an oral dose is excreted unchanged in the urine.	Excreted unchanged and as metabolites in urine.		0,05	0	0,05
Metoclopramide	A03FA01	10-20	15	It is excreted in the urine, about 85% of a dose being eliminated in 72 hours, 20% as unchanged metoclopramide and the remainder as sulfate or glucuronide conjugates, or as metabolites.About 5% of a dose is excreted in faeces via the bile.	80% of a dose excreted as unchanged drug and metabolites in urine.		0,2	0,05	0,25

Grontmij

stowa

planning connecting respecting the future

Inventory intake pharmaceuticals from care institutions



overzicht patiënten per farmacotherapeutische groep

Selecteer een afdeling

Vliedberg Hk 2 (VB2)

Klik op een kolomnaam om op die kolom te sorteren. Klik nogmaals om de sortering om te keren.

Totalen voor Vliedberg Hk 2 in de periode 20-10-2009 t/m 20-10-2009

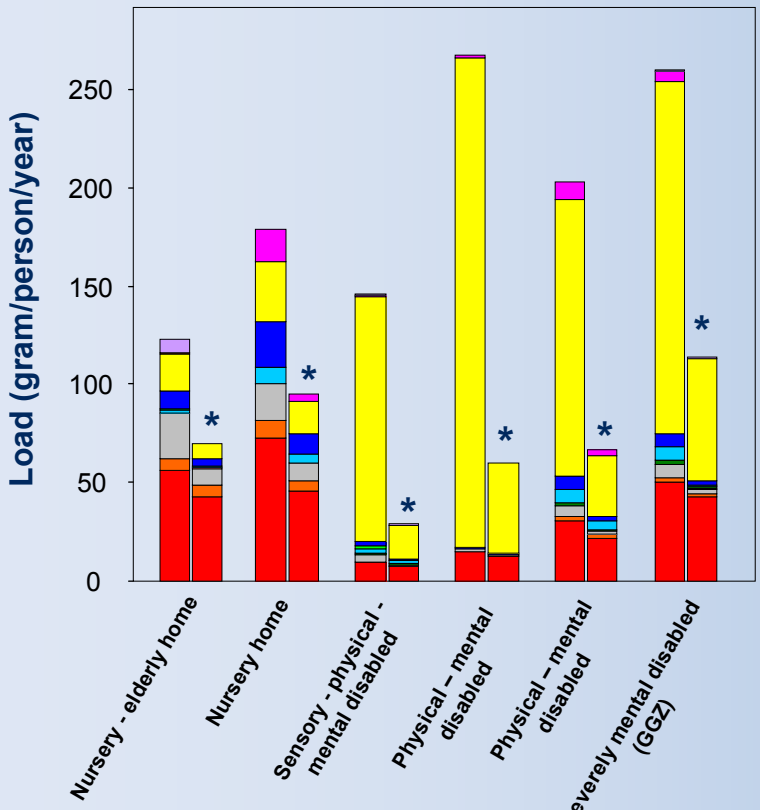
GPK	HPK	Generieke product naam	Aantal
20303		acenocoumarol tablet 1 mg	0,00 tabletten
65072		acetylcysteïne bruistablet 600 mg	2,00 bruistabletten
117153		acetylsalicylzuur dispertablet 30 mg	1,00 tabletten
117145		acetylsalicylzuur dispertablet 80 mg	1,00 tabletten
2224		allopurinol tablet 100 mg	1,00 tabletten
12467		allopurinol tablet 300 mg	1,00 tabletten
79197		amlodipine tablet 10 mg (besilaat)	1,00 tabletten
83712		atenolol tablet 25 mg	1,00 tabletten
14680		betamethason oplossing cutaan 0,5 mg/g	0,00 gram
66656		bisoprolol tablet 5 mg	1,00 tabletten
109525		bisoprolol tablet filmomhuld 2,5 mg	1,00 tabletten
13242		bumetanide tablet 1 mg	6,0 tabletten
39675		bumetanide tablet 5 mg	1,00 tabletten
113506		calciumcarbonaat/colecalciferol tablet 1,25 g (500 mg Ca)/400 IE	4,00 tabletten
82562		carbasalaatcalcium poeder 100 mg	4,00 zakjes
114901		carbomeer ooggel 2 mg/g (carbomeer 980)	2,00 centimeter
113603		ciprofloxacine tablet omhuld 500 mg	2,00 tabletten
101583		citalopram tablet omhuld 20 mg	1,00 tabletten
23086		codeïne tablet 10 mg (fosfaat)	1,00 tabletten

Grontmij

stowa

planning connecting respecting the future

Load (g/p/y): intake and calculated emission (*)

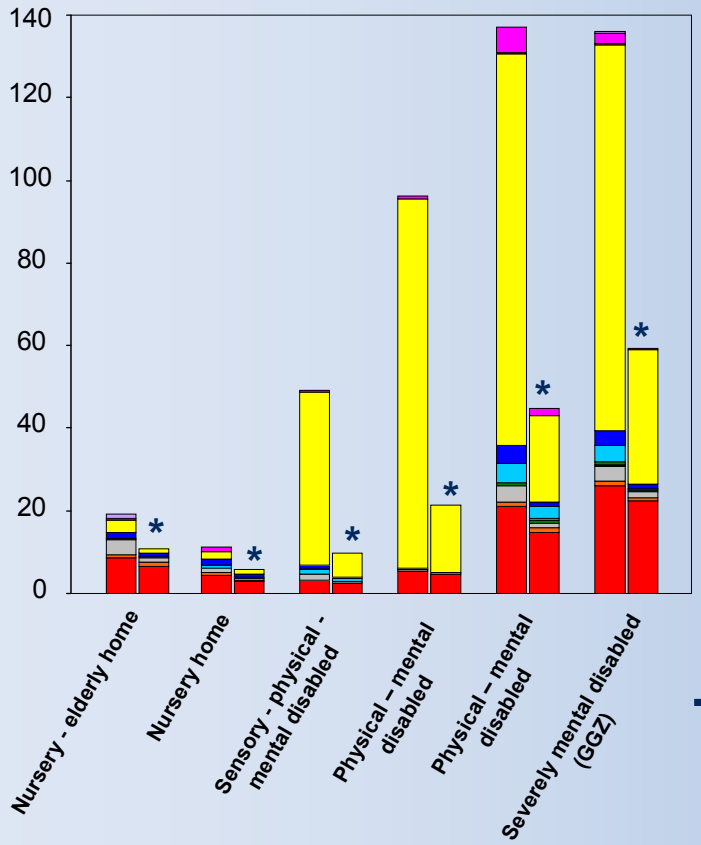


ATC CODE

- A - ALIMENTARY TRACT AND METABOLISM
- B - BLOOD AND BLOOD FORMING ORGANS
- C - CARDIOVASCULAR SYSTEM
- D - DERMATOLOGICALS
- G - GENITO URINARY SYSTEM AND SEX HORMONES
- H - SYSTEMIC HORMONAL PREPARATIONS
- J - ANTIINFECTIVES FOR SYSTEMIC USE
- L - ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS
- M - MUSCULO-SKELETAL SYSTEM
- N - NERVOUS SYSTEM
- P - ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS
- R - RESPIRATORY SYSTEM
- S - SENSORY ORGANS
- V - MISCELLANEOUS

- **Sensory-physical-mental disabled: N relevant**
- **Nursery / elderly homes: A and M relevant**

Load (kg/y): intake and calculated emission (*)



ATC CODE

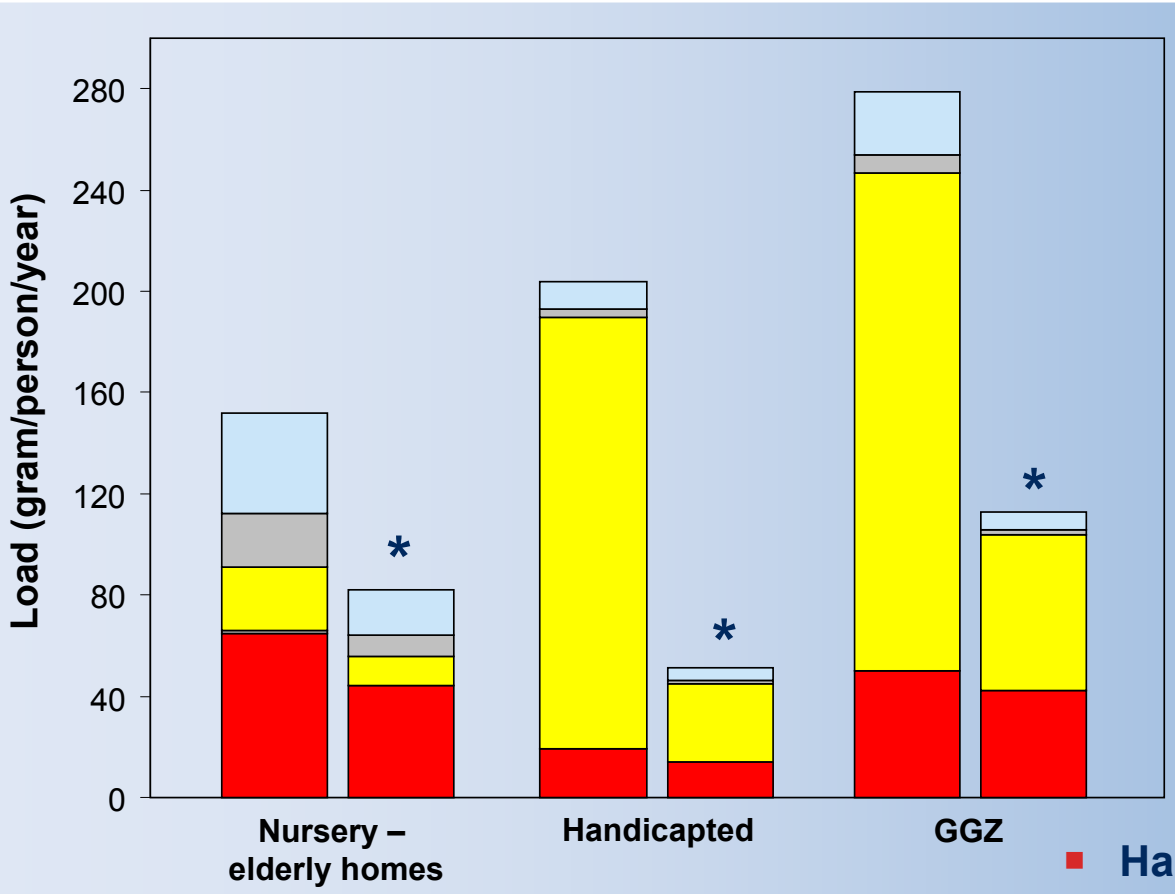
- A - ALIMENTARY TRACT AND METABOLISM
- B - BLOOD AND BLOOD FORMING ORGANS
- C - CARDIOVASCULAR SYSTEM
- D - DERMATOLOGICALS
- G - GENITO URINARY SYSTEM AND SEX HORMONES
- H - SYSTEMIC HORMONAL PREPARATIONS
- J - ANTIINFECTIVES FOR SYSTEMIC USE
- L - ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS
- M - MUSCULO-SKELETAL SYSTEM
- N - NERVOUS SYSTEM
- P - ANTIPARASITIC PRODUCTS, INSECTICIDES AND REPELLENTS
- R - RESPIRATORY SYSTEM
- S - SENSORY ORGANS
- V - MISCELLANEOUS

Total load pharmaceuticals depends on size (i.e. beds) of institution!

Load (g/p/y): calculated emission per active compound

Nursery and elderly homes		Severely mental disabled (GGZ)		Handicapted	
A10BA02 – Metformine	32,03	A10BA02 - Metformine	24,63	N03AX14 - Levetiracetam	15,83
B01AC07 – Dipyramidol	6,35	N05AN01 - Lithium	8,75	A10BA02 - Metformine	11,28
N03AX14 – Levetiracetam	4,62	N07BB03 - Acamprosaat	2,41	N03AF01 - Carbamazepine	5,09
C03CA01 – Furosemide	4,29	N03AG01 - Valproïnezuur	1,88	N05AD05 - Pipamperon	3,72
C07AA07 – Sotalol	1,89	N05AD05 - Pipamperon	1,85	J01CA04 - Amoxicilline	3,39
R05CB01 – Acetylcysteïne	1,3	N03AX14 - Levetiracetam	1,52	N03AG01 - Valproïnezuur	3,13
N03AX12 – Gabapentine	1,22	N05AH02 - Clozapine	1,08	N05AN01 - Lithium	1,85
M09AA01 – Hydrokinine	1,16	M01AE01 - Ibuprofen	0,97	N03AX12 - Gabapentine	1,71
A02BC05 – Esomeprazol	0,78	J01EE01 - Co-trimoxazol	0,96	V03AE02 - Sevelamer	1,62
A07EC02 – Mesalazine	0,77	J01CF05 - Flucloxacilline	0,77	N03AG04 - Vigabatrine	1,36
J01CR02 – Clavulaanzuur	0,76	N05AH04 - Quetiapine	0,74	J01CR02 - Clavulaanzuur	0,82
M01AE02 – Naproxen	0,73	N03AF01 - Carbamazepine	0,65	R05CB01 - Acetylcysteïne	0,66
J01XX05 – Methenamine	0,73	J01CA04 - Amoxicilline	0,6	B02AA02 - Tranexaminezuur	0,58
N03AX16 – Pregabaline	0,68	H03AA01 - Levothyroxine	0,54	B01AC07 - Dipyramidol	0,56
M05BX04 - Strontiumranelaat	0,62	B01AC07 - Dipyramidol	0,54	N03AX09 - Lamotrigine	0,54
J01MA02 – Ciprofloxacine	0,55	N05AF05 - Zuclopenthixol	0,43	A09AA02 - Pancreatine	0,45
C07AB02 – Metoprolol	0,52	N06AA10 - Nortriptyline	0,3	J01MA02 - Ciprofloxacine	0,45
C09CA01 – Losartan	0,49	N06AB04 - Citalopram	0,3	A02BC03 - Lansoprazol	0,38
C03AA03 – Hydrochlorothiazide	0,48	A02BC02 - Pantoprazol	0,28	N03AX16 - Pregabaline	0,36
M04AA01 – Allopurinol	0,46	M05BX03 - Strontiumranelaat	0,24	J01EE01 - Co-trimoxazol	0,35
A03FA03 – Domperidon	0,45	N05BA04 - Oxazepam	0,23	M03BX01 - Baclofen	0,32

Load (g/p/y) based on chemical analysis with and without excretion (*)



ATC-code

- A - ALIMENTARY TRACT AND METABOLISM
- C - CARDIOVASCULAR SYSTEM
- N - NERVOUS SYSTEM
- V - MISCELLANEOUS

- **Handicapted and GGZ: N relevant**
- **Nursery / elderly homes: A relevant**

Grontmij stowa planning connecting respecting the future

WTP removal rates pharmaceuticals

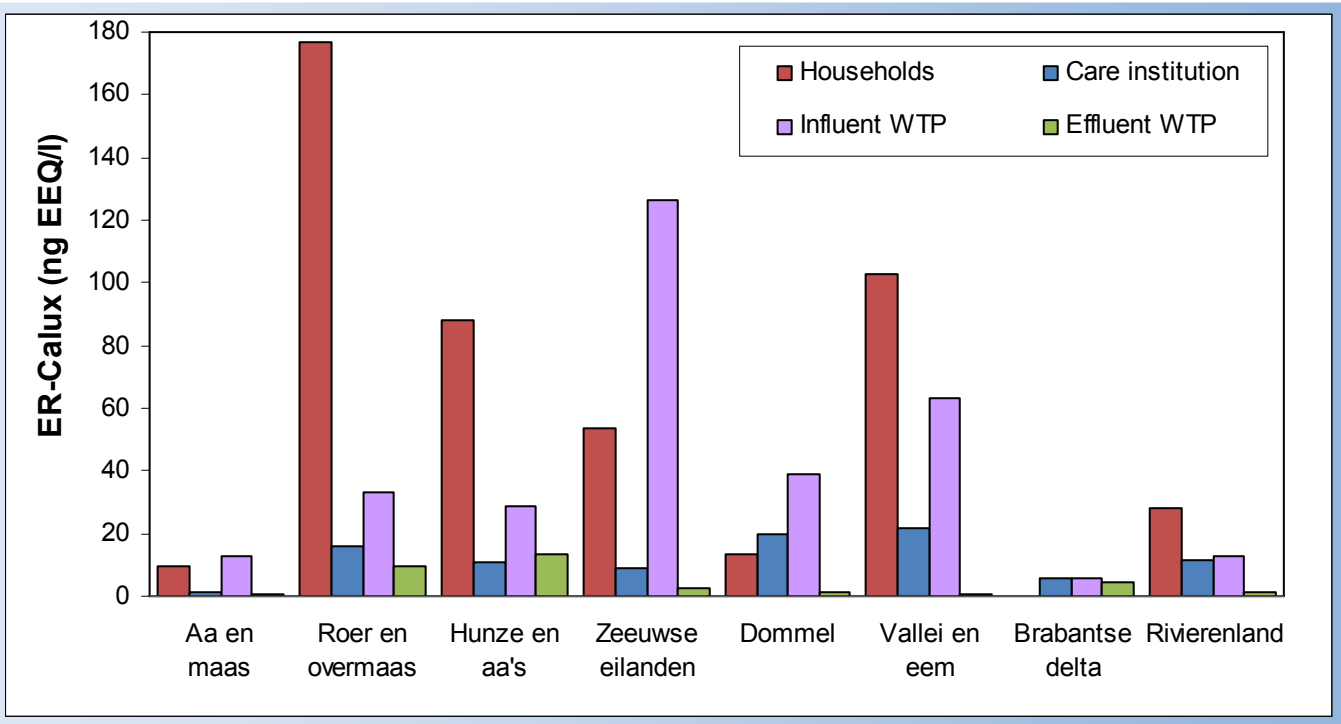
ATC Code	Compound	Removal rate (%)
A10BA02	Metformine	89
B01AC07	Dipyridamol	96
C01BB01	Lidocaïne	22
C03AB02	Bezafibraat	93
C07AA07	Sotalol	19
C07AB02	Metoprolol	26
C10AB02	Bezafibraat	64
C10AB04	Gemfibrozil	48
J01EA01	Trimethoprim	8
J01EC01	Sulfamethoxazol	76
J01FA10	Azitromycine	33
L01AA01	Cyclofosfamide	100
M01AB05	Diclofenac	29
M01AE01	Ibuprofen	96
M01AE02	Naproxen	84
M01AE03	Ketoprofen	49
N02BB01	Fenazon	100
N03AA03	Primidon	17
N03AF01	Carbamazepine	9
N03AX12	Gabapentine	15
N03AX14	Levetiracetam	84
N05AD05	Pipamperon	58
N05AH02	Clozapine	56
N05AH04	Quetiapine	87
N05AN01	Lithium	15
N05BA04	Oxazepam	18
V08AA05	Joxitalaminezuur	38
V08AB10	Jomeprol	75

Very differing removal rates!

Prioritisation based on environmental risk index Load / Defined Daily Dosis (DDD)

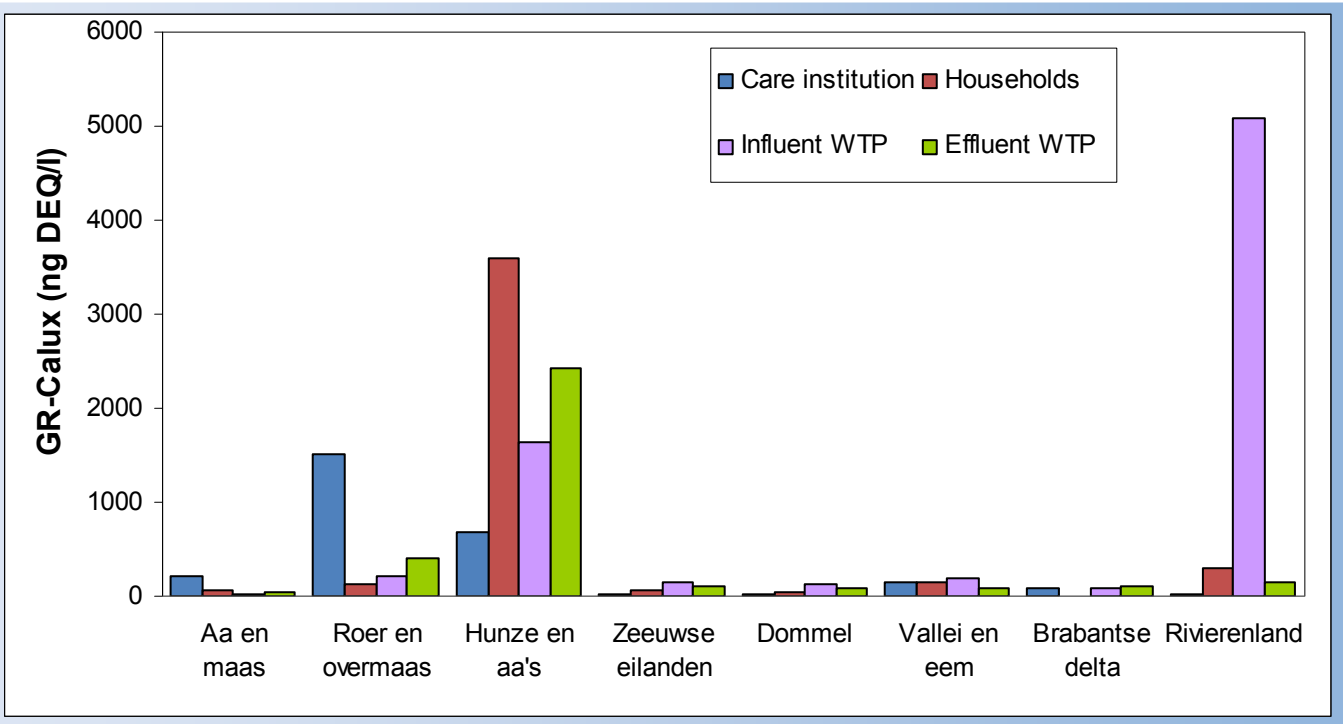
Pharmaceutical in effluent WTP	Environmental risk index	Waterboards	GWRC Class	RIVM Class
C07AB02 - Metoprolol	37,5	7	II	
N05BA04 - Oxazepam	20,3	7	III	
A10BA02 - Metformine	8,8	7	III	x
C07AA07 - Sotalol	8,5	7	II	x
N05AD05 - Pipamperon	7,2	5		
M01AB05 - Diclofenac	5,9	7	I	
N05AH02 - Clozapine	5,5	7		
C01BB01 - Lidocaïne	3,3	6		
N03AX12 - Gabapentine	2,9	7		x
N05AH04 - Quetiapine	1,8	5		
B01AC07 - Dipyridamol	1,5	4		
N03AF01 - Carbamazepine	1,3	7	I	
J01EA01 - Trimethoprim	1,2	5	II	
M01AE03 - Ketoprofen	1,2	4		
C10AB04 - Gemfibrozil	1,0	7	I	
M01AE02 - Naproxen	0,9	7	I	x
J01FA09 - Clarithromycine	0,5	1	II	x
N03AX14 - Levetiracetam	0,4	7		x
N03AA03 - Primidon	0,4	1		
C10AB02- Bezafibraat	0,3	6	I	
J01FA10 - Azitromycine	0,3	5		
M01AE01 - Ibuprofen	0,2	7	I	
C10AB05 - Fenofibraat	0,2	1		
J01EC01 - Sulfamethoxazol	0,2	3	I	x
N02BB01 - Fenazon	0,0	1		

ER-Calux: estrogen activity



- high removal rates in WTP
- care institutions: except ZE, lower activity than households
- households: RO, HA and VE high activity

GR-Calux: glucocorticoid activity



- differing removal rates in WTP
- care institutions: RO an HA high activity
- households: HA high activity

Research necessary for identification relevant compounds

TABLE 2. Concentration of Hormones in Extracts of Various Wastewaters Collected in The Netherlands

sample location (sampling date)	GR CALUX (ng dex EQs/L)	glucocorticoids	LC-MS/MS measured concentration[a] (ng/L)	relative potency (REP)[b]	predicted (total) dex EQs[c] (ng dex EQs/L)
Industry wastewater (12/05/2006; Van der Linden et al., 2008)		cortisol	13 ± 1 (80%)	0.07 ± 0.08	0.92 ± 1.1
		cortisone	26 ± 3 (80%)	<0.0008 ± 0.00006	max. 0.02 ± 0.1
		dexamethasone	90 ± 9 (89%)	1 ± 0.05	90.0 ± 0.1
		prednisolone	247 ± 28 (73%)	0.2 ± 0.1	49.3 ± 0.5
		prednisone	N.D. (77%)	-	-
		triamcinolone acetonide	N.D (74%)	-	-
	243 ± 32				Σ 140.2 ± 1.2
hospital wastewater 1 (12/11/2006; Van der Linden et al., 2008)		cortisol	275 ± 27 (80%)	0.07 ± 0.08	19.2 ± 1.1
		cortisone	381 ± 44 (80%)	<0.0008 ± 0.00006	max. 0.03 ± 0.8
		dexamethsone	N.D. (89%)	-	-
		prednisolone	315 ± 30 (73%)	0.2 ± 0.1	63.0 ± 0.5
		prednisone	117 ± 12 (77%)	<0.002 ± 0.0004	Max. 0.2 ± 0.2
		triamcinolone acetonide	41 ± 4 (74%)	2.3 ± 0.04	93.2 ± 0.1
	96 ± 13				Σ 176.7 ± 1.5
hospital wastewater 2 (8/19/2009)		cortisol	301 ± 29 (80%)	0.07 ± 0.08	21.1 ± 1.1
		cortisone	472 ± 54 (80%)	<0.0008 ± 0.00006	max. 0.4 ± 0.1
		dexamethasone	N.D. (89%)	-	-
		prednisolone	1918 ± 182 (73%)	0.2 ± 0.1	383.6 ± 0.5
		prednisone	545 ± 58 (77%)	<0.002 ± 0.0004	1.1 ± 0.2
		triamcinolone acetonide	14 ± 1 (74%)	2.3 ± 0.04	31.1 ± 0.1
	609 ± 79				Σ 437.2 ± 1.3
paper mill treated wastewater (01/15/2007; Van der Linden et al., 2008)		cortisol	N.D. (80%)	-	-
		cortisone	N.D. (80%)	-	-
		dexamethasone	N.D. (89%)	-	-
		prednisolone	N.D. (73%)	-	-
		prednisone	N.D. (77%)	-	-
		triamcinolone acetonide	N.D. (74%)	-	-
	11 ± 2				0
sewage treatment plant effluent (11/15/2006; Van der Linden et al., 2008)		cortisol	N.D. (80%)	-	-
		cortisone	N.D. (80%)	-	-
		dexamethasone	N.D. (89%)	-	-
		prednisolone	N.D. (73%)	-	-
		prednisone	N.D. (77%)	-	-
		triamcinolone acetonide	14 ± 1 (74%)	2.3 ± 0.04	31.1 ± 0.1
	38 ± 13				Σ 31.1 ± 0.1

High-Resolution Mass Spectrometric Identification and Quantification of Glucocorticoid Compounds in Various Wastewaters in The Netherlands

MERIJN SCHRIKS,*,† JAN A. VAN LEERDAM,† SANDER C. VAN DER LINDEN,‡ BART VAN DER BURG,‡ ANNEMARIE P. VAN WEZEL,† AND PIM DE VOOGT†,§

KWR Watercycle Research Institute, Nieuwegein, The Netherlands, BioDetection Systems B.V., Amsterdam, The Netherlands, and Institute for Biodiversity and Ecosystem Dynamics, University of Amsterdam, Amsterdam, The Netherlands

Received January 4, 2010. Revised manuscript received May 3, 2010. Accepted May 11, 2010.

Ecotoxicological risk assessment (PEC/PNEC)

Active compound	Species	Endpoint		PEC / PNEC							
				Aa en Maas	Roer en Overmaas	Hunze en Aa's	Scheldestromen	Dommel	Vallei en Eem	Brabantse Delta	Rivierenland
			EC50 (µg/l)								
Carbamazepine	Glomus intraradices (Mycorrhizal fungus)	Spore production	43,6							0,3	
Clarithromycine	Pseudokirchneriella subcapitata (Green algae)	growth inhibition	2,0			0,1					
			NOEC (µg/l)								
Diclofenac	Oncorhynchus mykiss (rainbow trout)	renal lesions and alterations of the gill	1,0	0,4	0,5	0,4	0,2	0,4	0,4	0,3	0,1
Diclofenac	Salmo trutta f. fario (Fish)	monocyte infiltration/accumulation in liver	0,5	0,8	1,0	0,8	0,4	0,8	0,8	0,6	0,1
Ibuprofen	Selenastrum capricornutum (Freshwater green algae)	growth inhibition	10,0							0,1	
Carbamazepine	Ceriodaphnia dubia (Crustacean cladocera)	reproduction	25,0							0,6	
Carbamazepine	Ceriodaphnia dubia (Crustacean cladocera)	reproduction inhibition	25,0							0,6	
			LOEC (µg/l)								
Metoprolol	Oncorhynchus mykiss (Rainbow trout)	liver, ultrastructural effects	1,0	2,8	3,2	2,1	1,7	2,8	3,0	1,6	2,5
Metoprolol	Oncorhynchus mykiss (Rainbow trout)	gills, ultrastructural effects	20,0	0,1	0,2	0,1	0,1	0,1	0,2	0,1	0,1
Gemfibrozil	Carassius auratus (Goldfish)	decrease in plasma testosterone	1,5	0,1	0,2	1,2	0,2	0,1	0,2	0,1	0,2
Diclofenac	Oncorhynchus mykiss (rainbow trout)	renal lesions and alterations of the gill	5,0	0,1	0,1	0,1	0,0	0,1	0,1	0,1	
Diclofenac	Oncorhynchus mykiss (rainbow trout)	cytological alterations in liver, kidney and gills	1,0	0,4	0,5	0,4	0,2	0,4	0,4	0,3	0,1
Diclofenac	Oryzias latipes (Japanese medaka)	induction of CYP1A, p53 gene and VTG	1,0	0,4	0,5	0,4	0,2	0,4	0,4	0,3	0,1
Diclofenac	Oncorhynchus mykiss (Rainbow trout)	gills, ultrastructural effects	1,0	0,4	0,5	0,4	0,2	0,4	0,4	0,3	0,1
Diclofenac	Oncorhynchus mykiss (Rainbow trout)	liver, ultrastructural effects	1,0	0,4	0,5	0,4	0,2	0,4	0,4	0,3	0,1
Diclofenac	Oncorhynchus mykiss (Rainbow trout)	kidney, ultrastructural effects	1,0	0,4	0,5	0,4	0,2	0,4	0,4	0,3	0,1
Ibuprofen	Synechocystis sp. PCC6803 (Cyanobacteria)	growth inhibition	1,0	0,1	0,6	0,2	0,2	0,1	0,1	0,6	0,1
Ibuprofen	Riverine biofilm community	decrease in cyanobacterial biomass	10,0		0,1					0,1	
Ibuprofen	Riverine biofilm community	carbohydrate utility spectra	10,0		0,1					0,1	
Ibuprofen	Riverine biofilm community	increased bacterial counts (R2A media)	10,0		0,1					0,1	
Ibuprofen	Riverine biofilm community	increase in actinomycete populations	10,0		0,1					0,1	
Ibuprofen	Riverine biofilm community	increase in fungal populations	10,0		0,1					0,1	
Ibuprofen	Riverine biofilm community	increase in beta proteobacteria and decrease in gamma proteobacteria	10,0		0,1					0,1	
Ibuprofen	Riverine biofilm community	increase in cytophaga-flavobacteria probe positive cells	10,0		0,1					0,1	
Ibuprofen	Riverine biofilm community	increase in alpha proteobacteria	10,0		0,1					0,1	
Ibuprofen	Riverine biofilm community	increase in SRB 385 probe positive cells	10,0		0,1					0,1	
Ibuprofen	Hydra vulgaris (Cnidarian)	partially contracted polyp, slow reactions	10,0		0,1					0,1	
Ibuprofen	Hydra vulgaris (Cnidarian)	mean number of Artemia ingested	10,0		0,1					0,1	
Ibuprofen	Oryzias latipes (Japanese medaka)	reproduction (no of eggs and no of days for reproduction)	1,0	0,1	0,6	0,2	0,2	0,1	0,1	0,6	0,1
Carbamazepine	Riverine biofilm community	decrease in bacterial biomass	10,0	0,1			0,1	0,1	0,1	1,5	
Carbamazepine	Riverine biofilm community	decrease in cyanobacterial biomass	10,0	0,1			0,1	0,1	0,1	1,5	
Carbamazepine	Riverine biofilm community	carbohydrate utility spectra	10,0	0,1			0,1	0,1	0,1	1,5	
Carbamazepine	Riverine biofilm community	increased bacterial counts (R2A media)	10,0	0,1			0,1	0,1	0,1	1,5	
Carbamazepine	Riverine biofilm community	increase in fungal populations	10,0	0,1			0,1	0,1	0,1	1,5	
Carbamazepine	Riverine biofilm community	increase in beta proteobacteria and decrease in gamma proteobacteria	10,0	0,1			0,1	0,1	0,1	1,5	
Carbamazepine	Riverine biofilm community	increase in LGC354c and HGC69a probe positive cells	10,0	0,1			0,1	0,1	0,1	1,5	
Carbamazepine	Cyprinus carpio (Common carp)	kidney, ultrastructural effects	1,0	0,6	0,4	0,4	0,6	0,6	0,7	15,0	0,5
Carbamazepine	Ceriodaphnia dubia (Crustacean cladocera)	reproduction inhibition	100,0							0,2	

Relative contributions (%) of pharmaceutical loads from care institutions to influent WTP

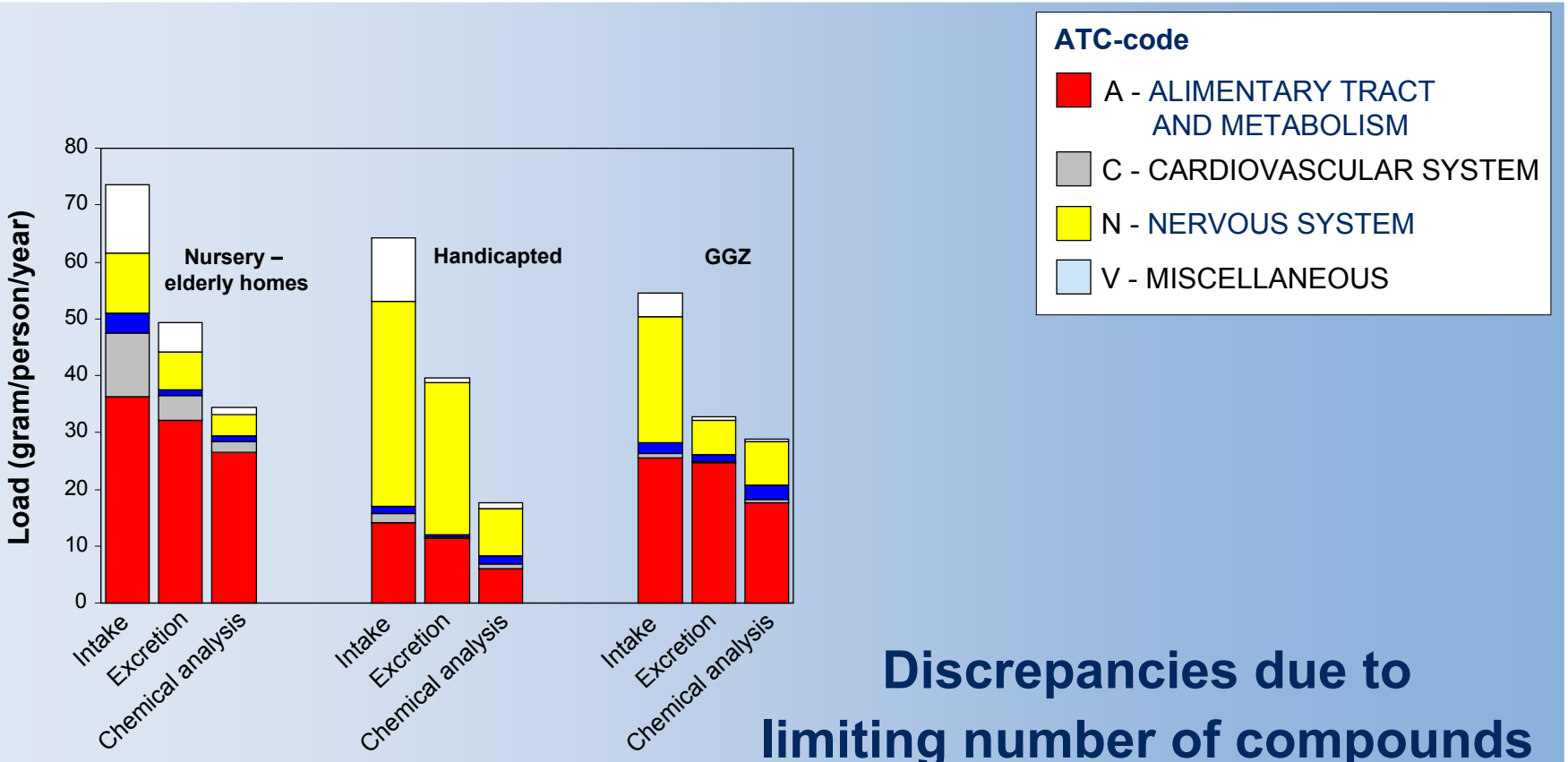
Compound	Nursery and elderly home WTP Stadskanaal	Nursery and elderly home WTP Simpelveld	Nursery home WTP Land van Ciujk	Nursery home WTP Tholen	GGZ WTP Amersfoort	GGZ WTP Eindhoven	Physical disabled WTP Groesbeek Breedeweg
Bezafibraat			3,3		3,1		
Carbamazepine			1,1		1,3		4,5
Clofibraat							2,6
Clozapine			**19,6**		**36**	**19,5**	
Diclofenac	1,4						1,5
Dipyridamol		**93**		1,2			
Gabapentine					4		4,5
Gemfibrozil				**8,8**		**6,6**	
Levetiracetam	1,7					**7,5**	**14,8**
Lidocaïne	2,7						
Lithium					2,1		
Metformine	1,1	**6,2**			1,2		
Metoprolol		2,6					
Naproxen					1,3		1,9
Oxazepam		**12,1**		1,8	**7,4**		
Pipamperon					**12**		
Quetiapine			2,1		**12**	**5**	
Sotalol		**10,6**		3			
Sulfamethoxazol					**7,4**	1,7	
Trimethoprim				**5,2**	1,6		**7,7**

Grontmij

stowa

planning connecting respecting the future

Comparison loads based on intake, excretion and chemical analysis



Discrepancies due to limiting number of compounds chemically analyzed

Identified priorty pharmaceuticals

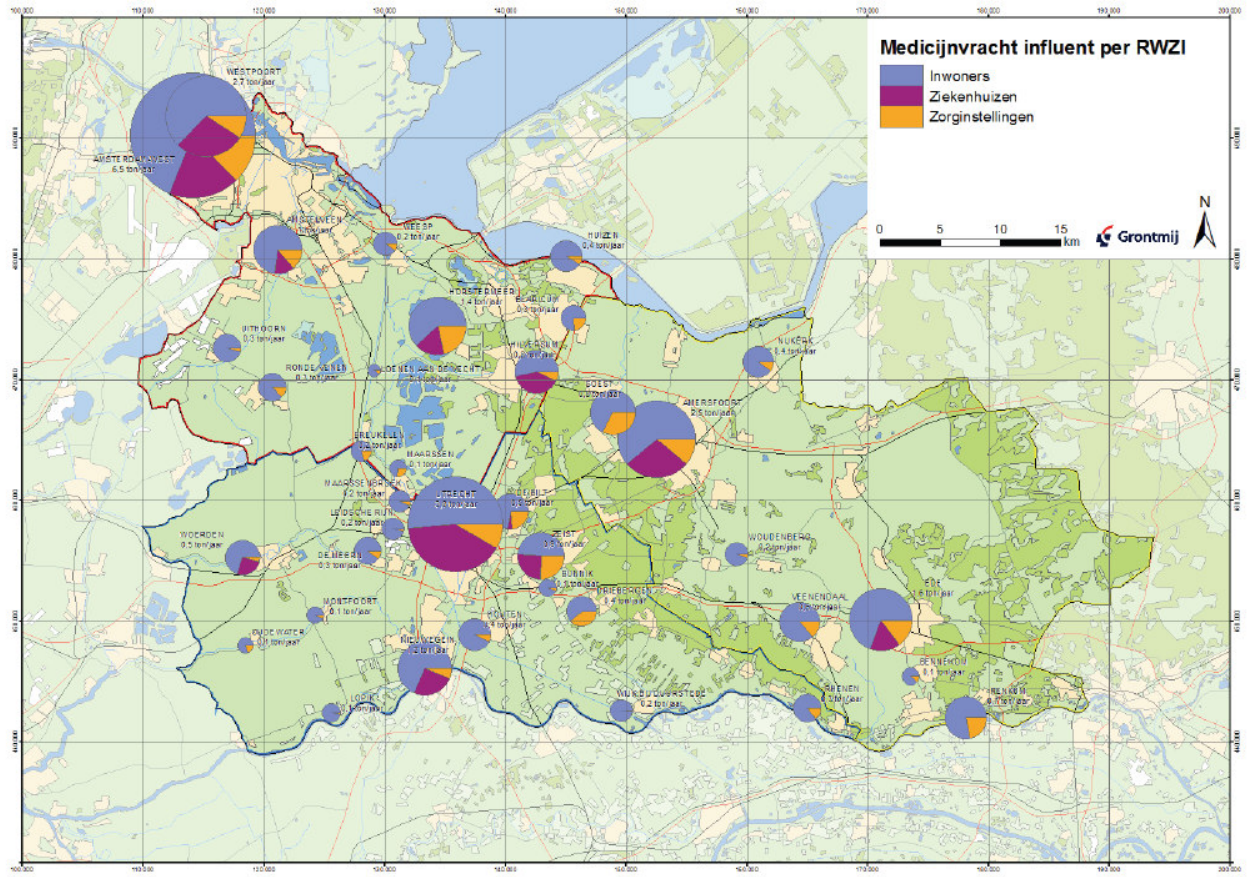
- A (alimentary tract and metabolism): metformine
- B (blood and blood forming organs): dipyramidol
- C (cardiovascular system): metoprolol, sotalol, gemfibrozil, lidocaïne
- M (muskulo-skeletal systeem): naproxen, diclofenac
- N (nervous system): gabapentine, oxazepam, pipamperon, carbamazepine, clozapine, levetiracetam, quetiapine

Conclusions & recommendations

- Care institutions may be relevant source of pharmaceutical emissions, but location and compound specific!
- Additional chemical monitoring at care institutions not necessary for investigated compounds: good correlations
- But number of measurable pharmaceuticals at laboratories need to be larger!
- Analysis methods need to be improved (LOQ)
- More research on pharmaceuticals belonging to N group
- Improved ecological risk assessment of pharmaceuticals necessary
- Assessment of identification and contribution of compounds to estrogen and glucocorticoid activity
- WFD needs to expand priorty list with e.g. metoprolol, sotalol, gabapentine, pipamperon en oxazepam

Outlook: GIS and dilution factors…

Aandeel type instelling per rwzi



Grontmij

stowa

planning connecting
respecting
the future

Questions?