Emission of pharmaceuticals from care units into wastewater: from identification of sources to monitoring

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Pharmaceuticals and environment: lots of attention!

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Introduction

Why research on pharmaceuticals necessary?

- Not a priority compound in WFD! Still no environmental threshold values…
- Large diversity pharmaceuticals:

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

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

Introduction

Information necessary about:

intake in The Netherlands, occurrence in aquatic environment, ecotoxicity, measures for reduction emission, identification discharge routes, bioavailability

Many types of human pharmaceuticals:

- Anti-depressives
- ß-blockers
- Anti-epileptics
- Analgetics
- Antibiotics
- X-ray contrast compounds
- Hormones
- Cholesterol reducing compounds
- ...

Introduction

- Wat is main emissionroute human pharmaceuticals?
  - Effluents from wastewater treatment plants (WTP's)
- Why a problem?
  - Possible negative effects on aquatic community (e.g. endocrine disruption)
  - Contamination of drinking water for human consumption
- What should be done?
  - Identification emission hot-spots!

Introduction

- Ministry of Housing, Spacial Planning and the Environment (VROM):

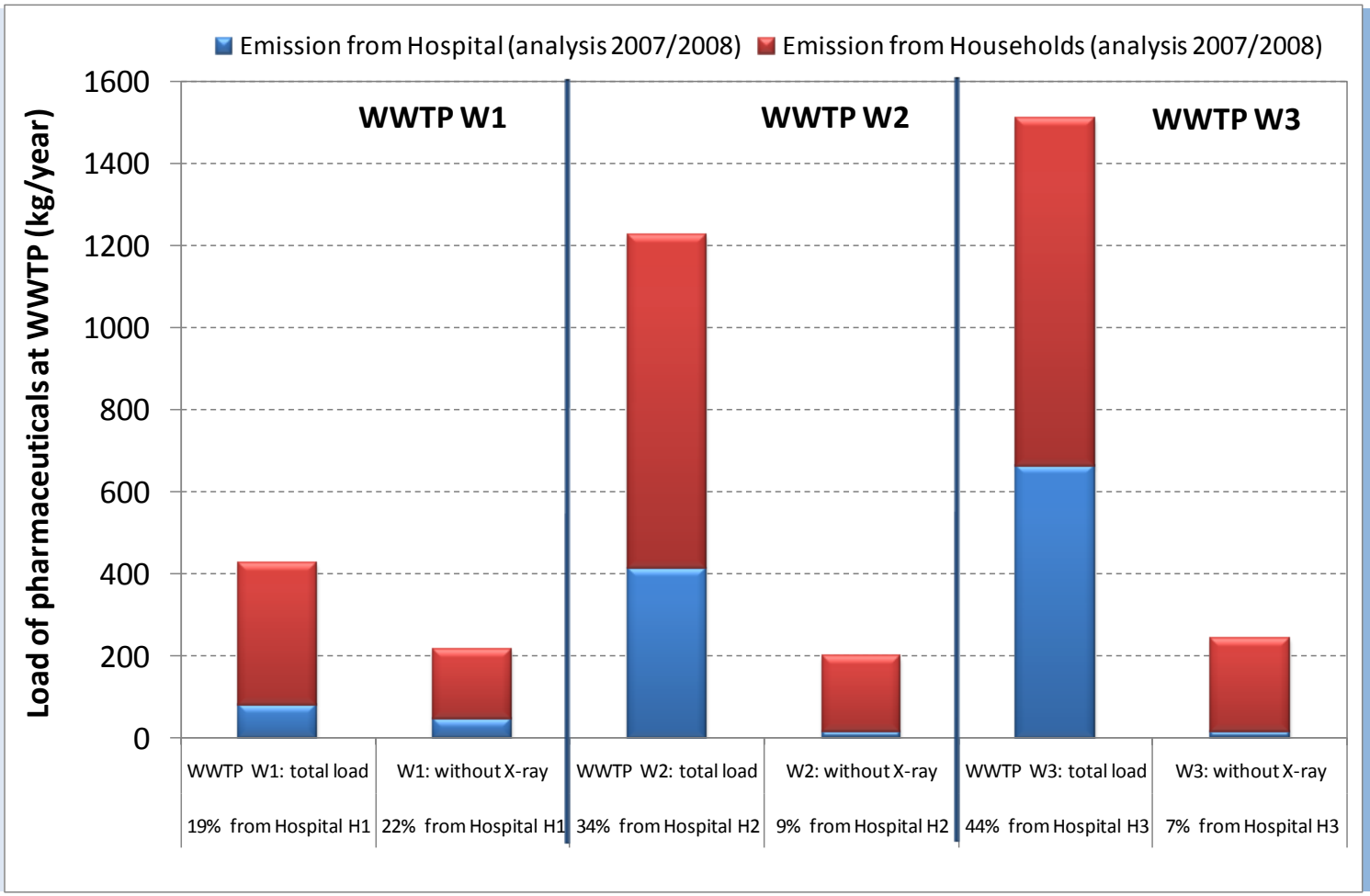
2006: “research needs to be performed on how to implement cost-effective measures for emission reduction for hospitals and care institutions”

Emissiereductie uit zorginstellingen	– Uitvoeren van haalbaarheidstudie en pilots naar emissiereducerende maatregelen in ziekenhuizen en zorginstellingen.

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 in order to make recommendations on cost-effective measures for discharge reductions
- **Funding:** STOWA (Foundation for Applied Water Research)

Loads of pharmaceuticals at WWTP



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Main conclusions

- Bulk emission from hospitals are 50-70 compounds
- X-ray contrast compounds (>50%) and antibiotics most relevant pharmaceuticals discharged by hospitals
- Comparison with estimated discharge household
  Locationspecific!
  - Prescriptions: 17-55% from hospital
  - Chemical measurements: 19-44% from hospital

- What is the emission of pharmaceuticals from the remaining care institutions?

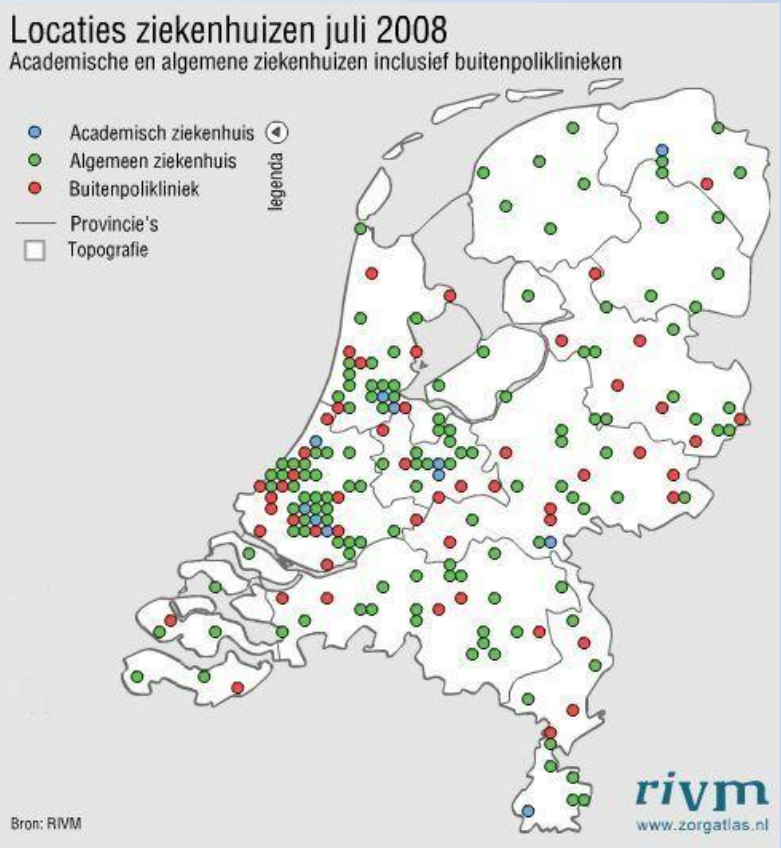
ZORG project (2009): CARE INSTITUTIONS

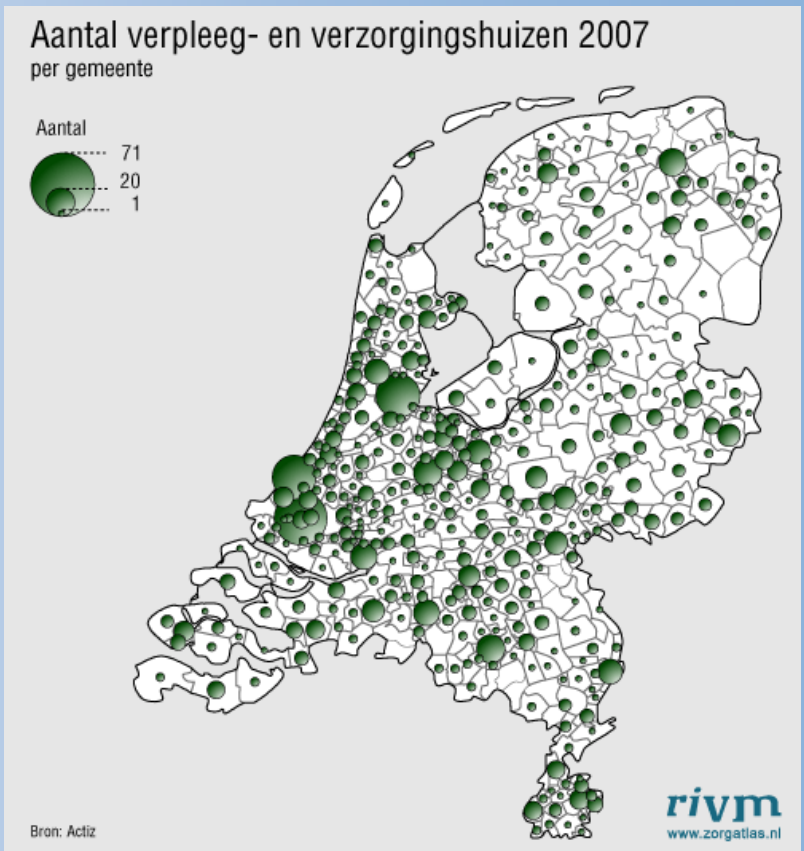
- **Aim:**
  - Collect data on nature and extent of pharmaceutical emissions from care institutions
  - Gather information for discussions on cost-effective measures for emission reduction
- **Set-up**
  - A. Literature study
  - B. Chemical and effect measurements wastewater
- **Funding:** STOWA (Foundation for Applied Water Research) and participation of 7 different waterboards

- A Literature study
  - Description types of care institutions
  - Numbers of locations, beds and patients
  - Use and intake pharmaceuticals
  - Ecotoxicological effects
  - Selection criteria for monitoring sites wastewater
  - Development pharmaceutical trends

- Identified care institutions:
  - Home for the elderly
  - Nursery homes
  - Physical disabled
  - Mental disabled
  - Sensory disabled
  - Severely mental disabled (GGZ)
  - Care institutions for addictions

Hospitals and nursing/elderly homes in The Netherlands





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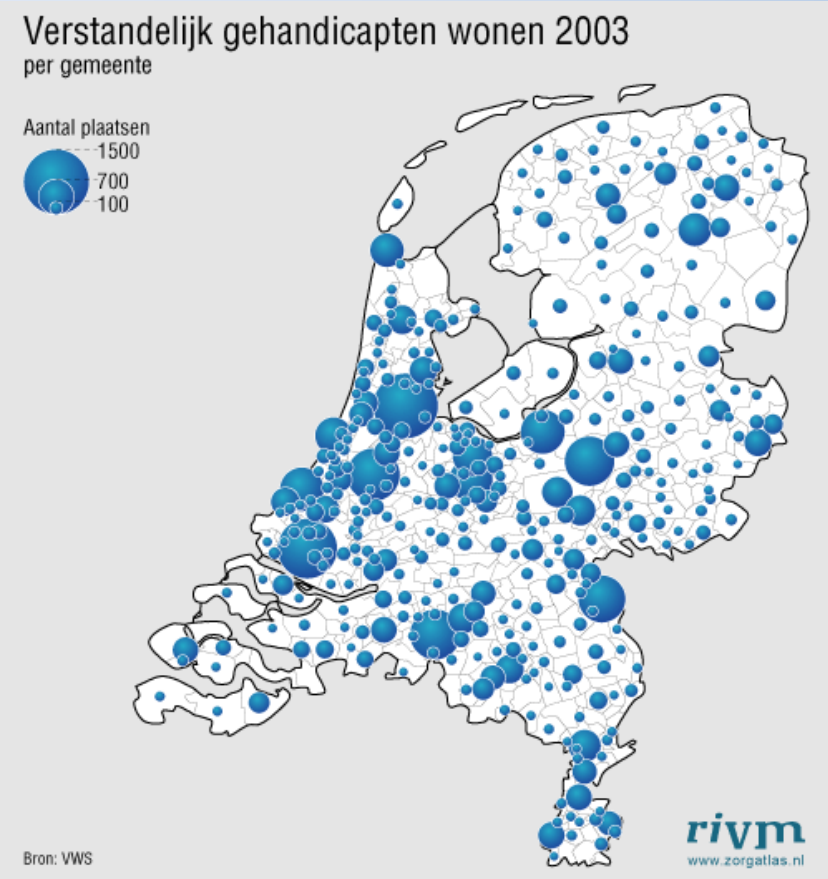
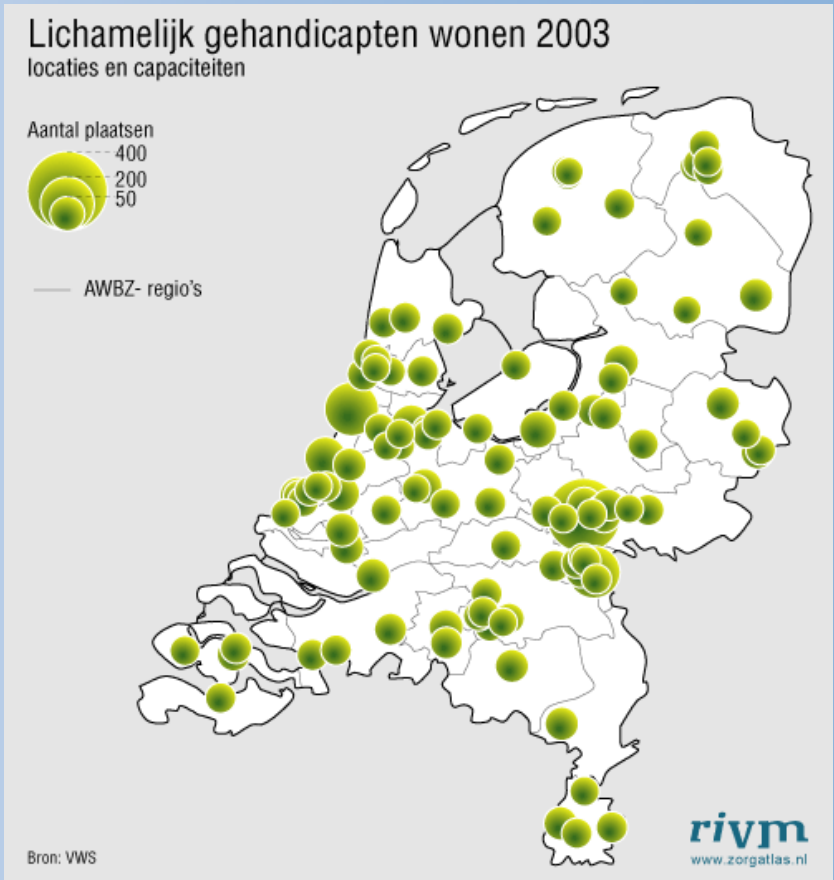
Mental and physical disabled in The Netherlands





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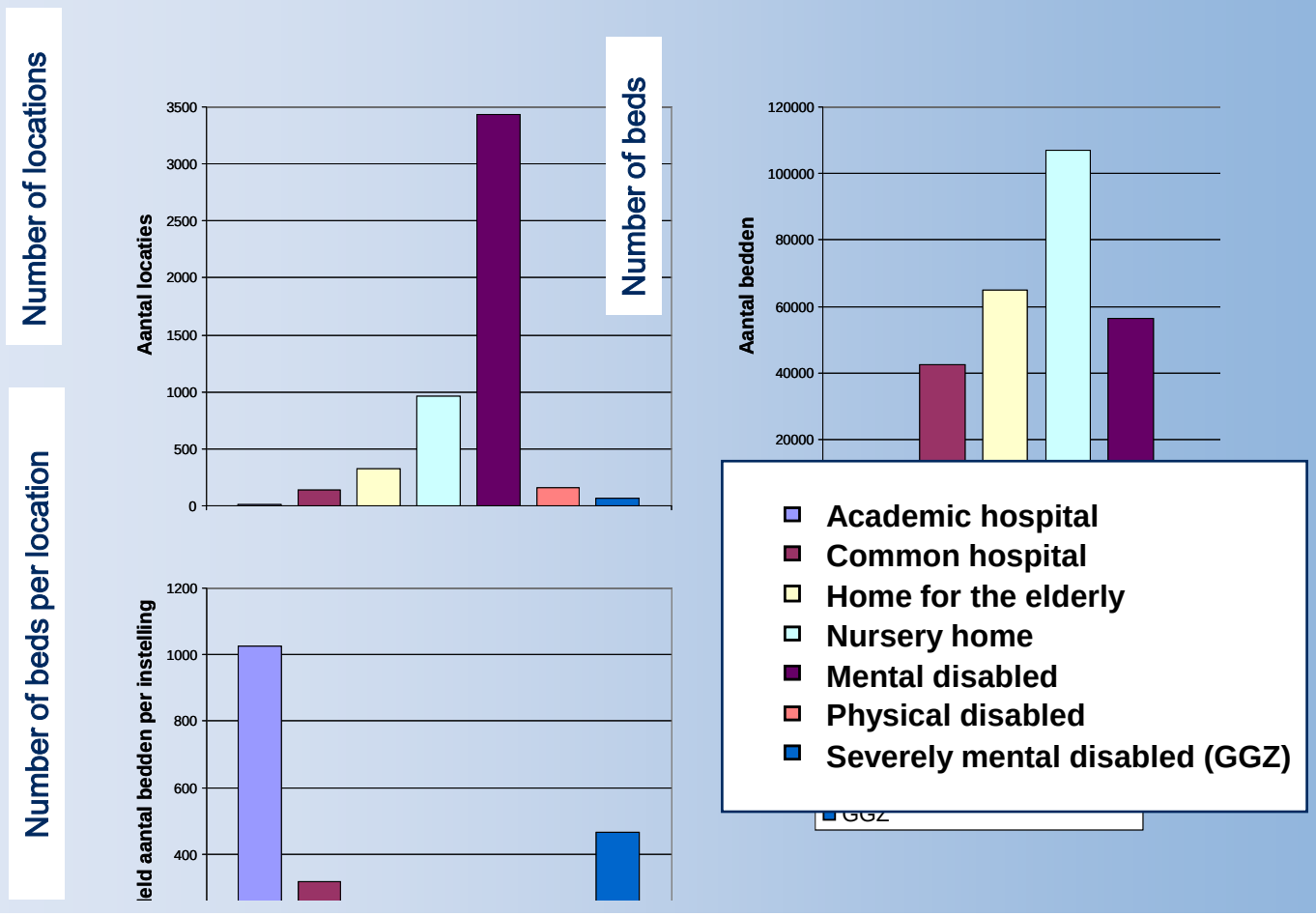
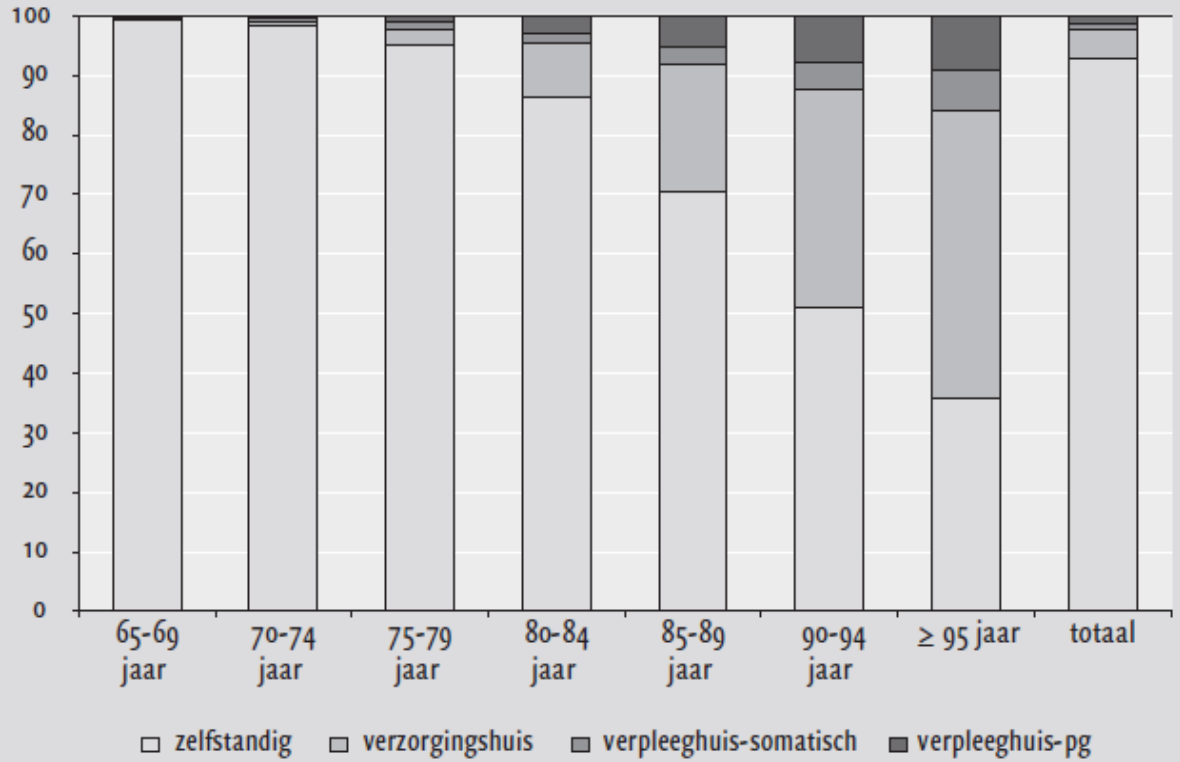
Number of locations and (average) beds per type of care institution



How do people live?



Bron: CBS (StatLine); Prismant/Arcares (2002)

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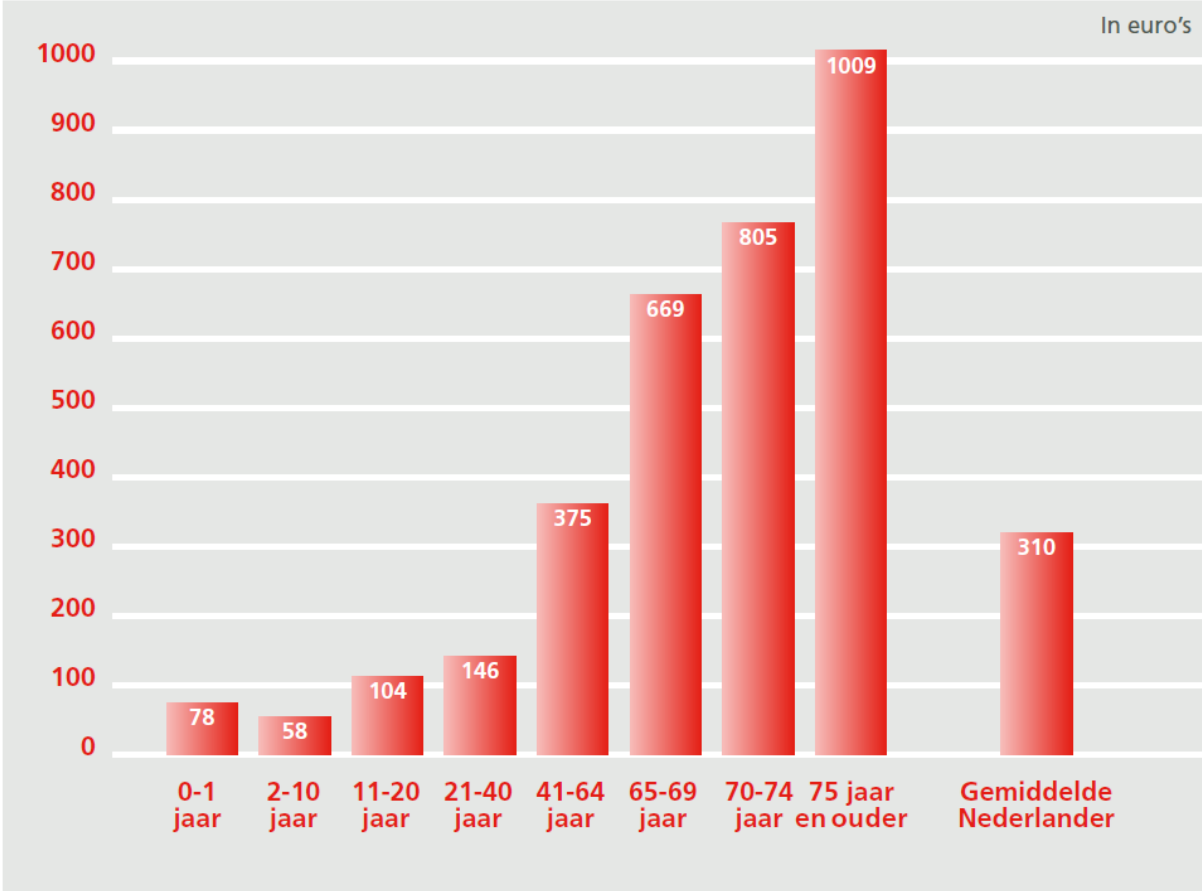
Intake pharmaceuticals by age



Bron: Stichting Farmaceutische Kengetallen

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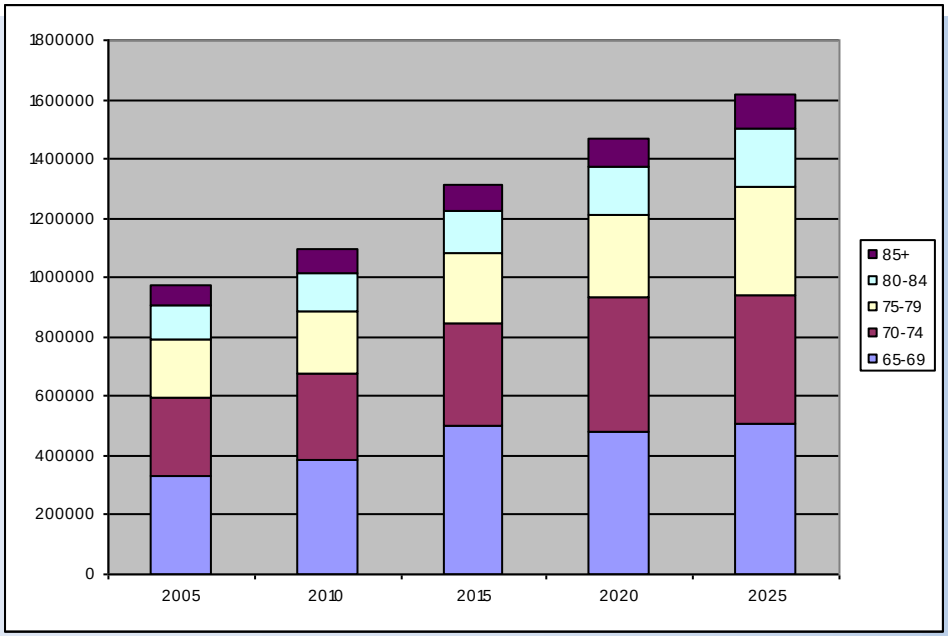
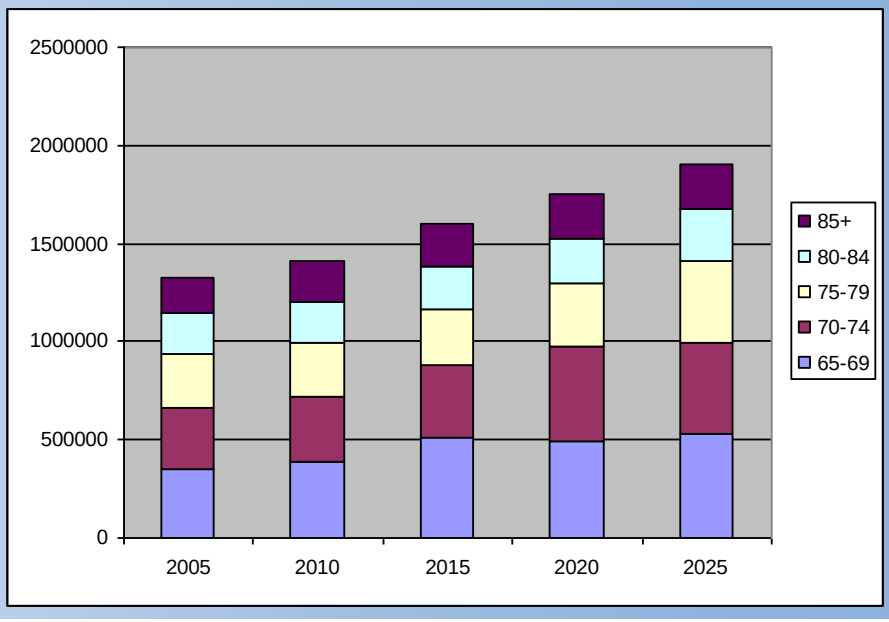
Demographic trends >65 jaar



1.6 million males in 2025

1.9 million females in 2025



Increased use pharmaceuticals expected!

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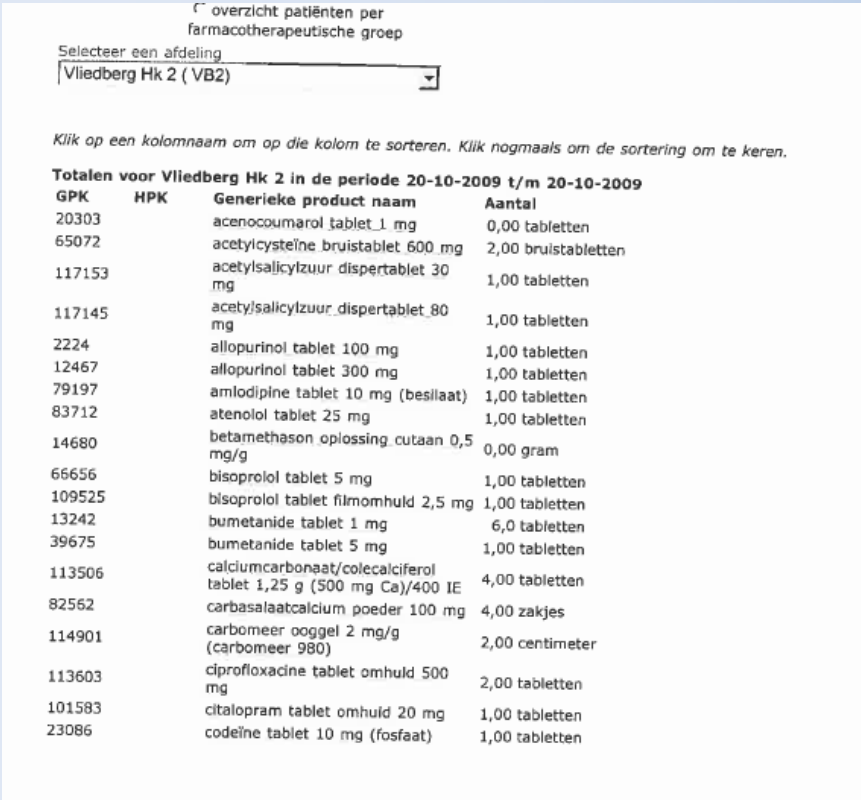
Results inventory intake pharmaceuticals from care institutions

Prescriptions



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

- **Estimation of:**
  - Load per institution
  - Load per person per institution
  - Load with incorporation excretion factors
  - Load with incorporation environmental risk-index: Defined Daily Dosis

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Approached care institutions: 10

	Name of institution	Location	Type of institution	# Residents	Format data	Time span
1	Zorggroep Reinalda	Haarlem	Home for the elderly / nursery home	155	Prescription	7 days
2	De Schoel	Sleen	Home for the elderly	27	Intake	1 day
3	De Lisse	Asten	Home for the elderly	62	Prescription	12 months
4	Ambachtshuys	Meppel	Mental disabled	5	Intake	1 day
5	Zorgboerderij Anderen	Anderen	Mental disabled	10	Intake	1 day
6	Robert Coppes Stichting	Vught	Sensory disabled	7	Intake	1 day
7	Bartimeus	Zeist	Sensory / mental / physical disabled	338	Prescription	6 months
8	Esdégé-reigersdaal	Heerhugowaard	Mental / physical disabled	360	Prescription	1 month
9	Het Dorp	Arnhem	Physical disabled	675	Prescription	14 days
10	Ziekenhuis Gelderse Vallei	Wolfheze	Severely mental disabled (GGZ)	524	Sales	12 months

Establisment 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	600-3000	1500	The majority of a dose of metronidazole is excreted in the urine, mainly as metabolites; a small amount appears in the faeces.	50 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	25	Corticosteroids are metabolised mainly in the liver but also in other tissues, and are excreted in the urine.					1
Hydrocortisone	A01AC03	20-500	250	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
Ranitide	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	0,38	0,26	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	A02BC06								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
ScopolaminebutylHyoscine 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
				The main metabolic pathways are N-dealkylation by	Mainly excreted in urine as metabolites				

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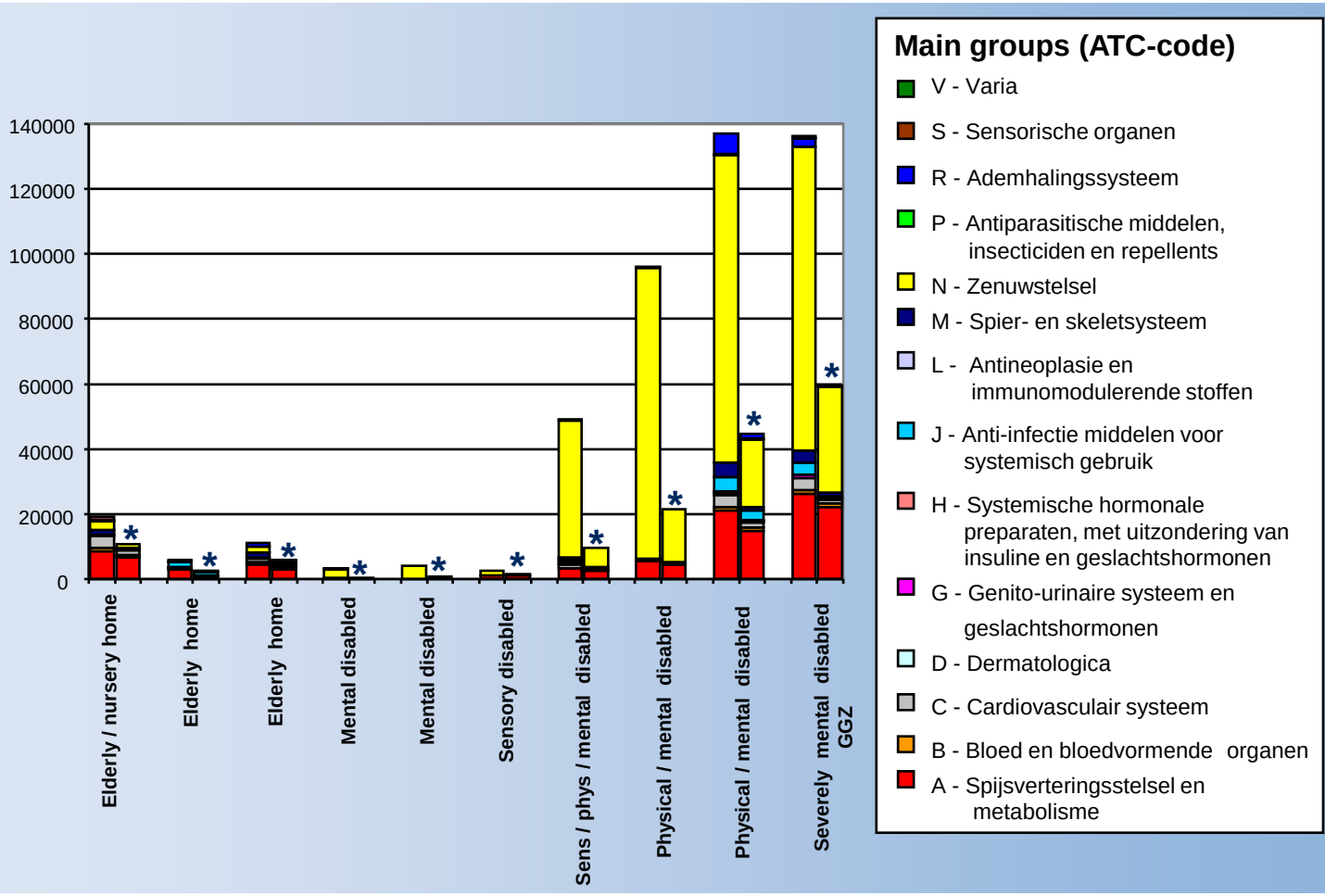
Total load in gram per year with and without excretion (*)



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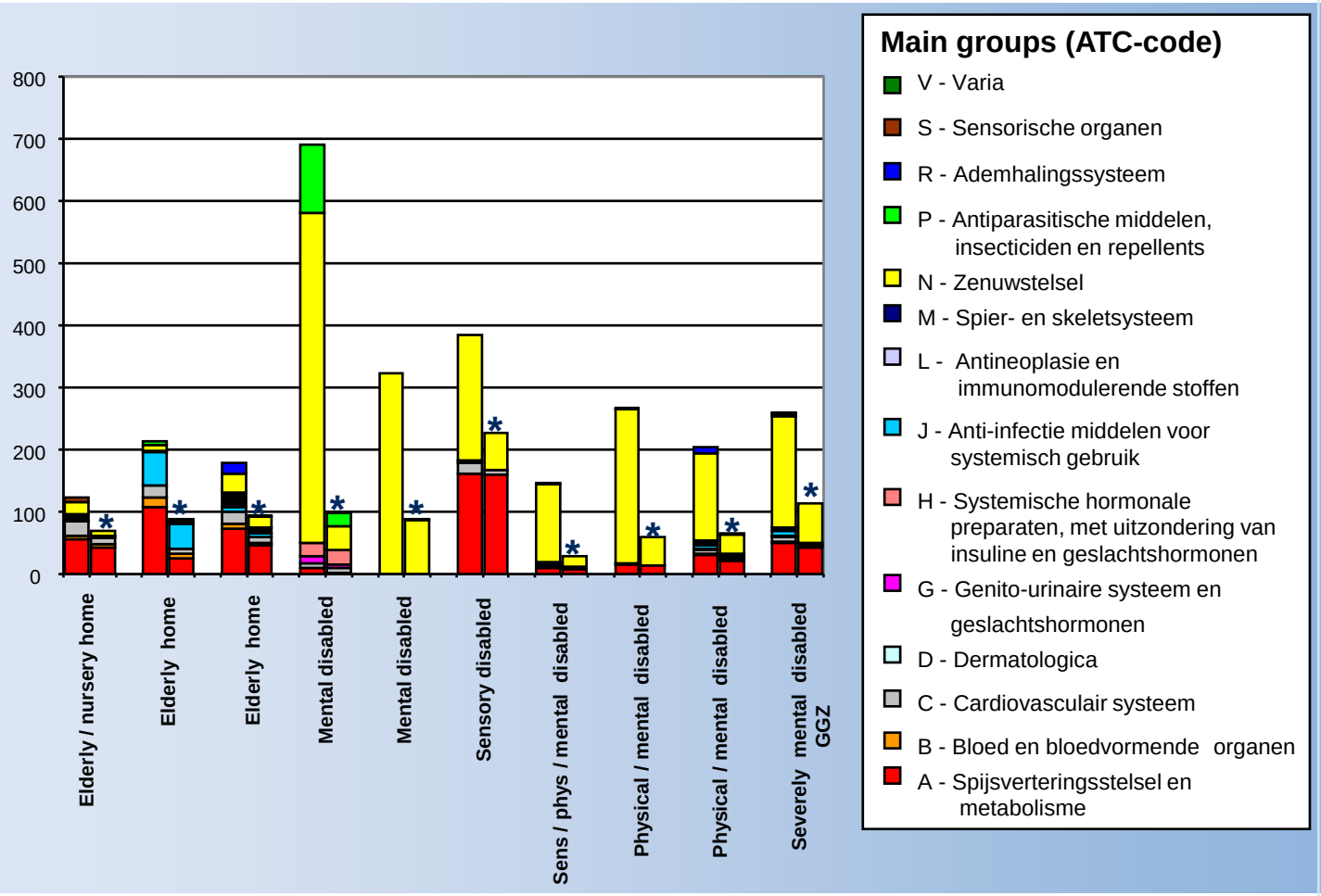
Total load in gram per person per year with and without excretion (*)



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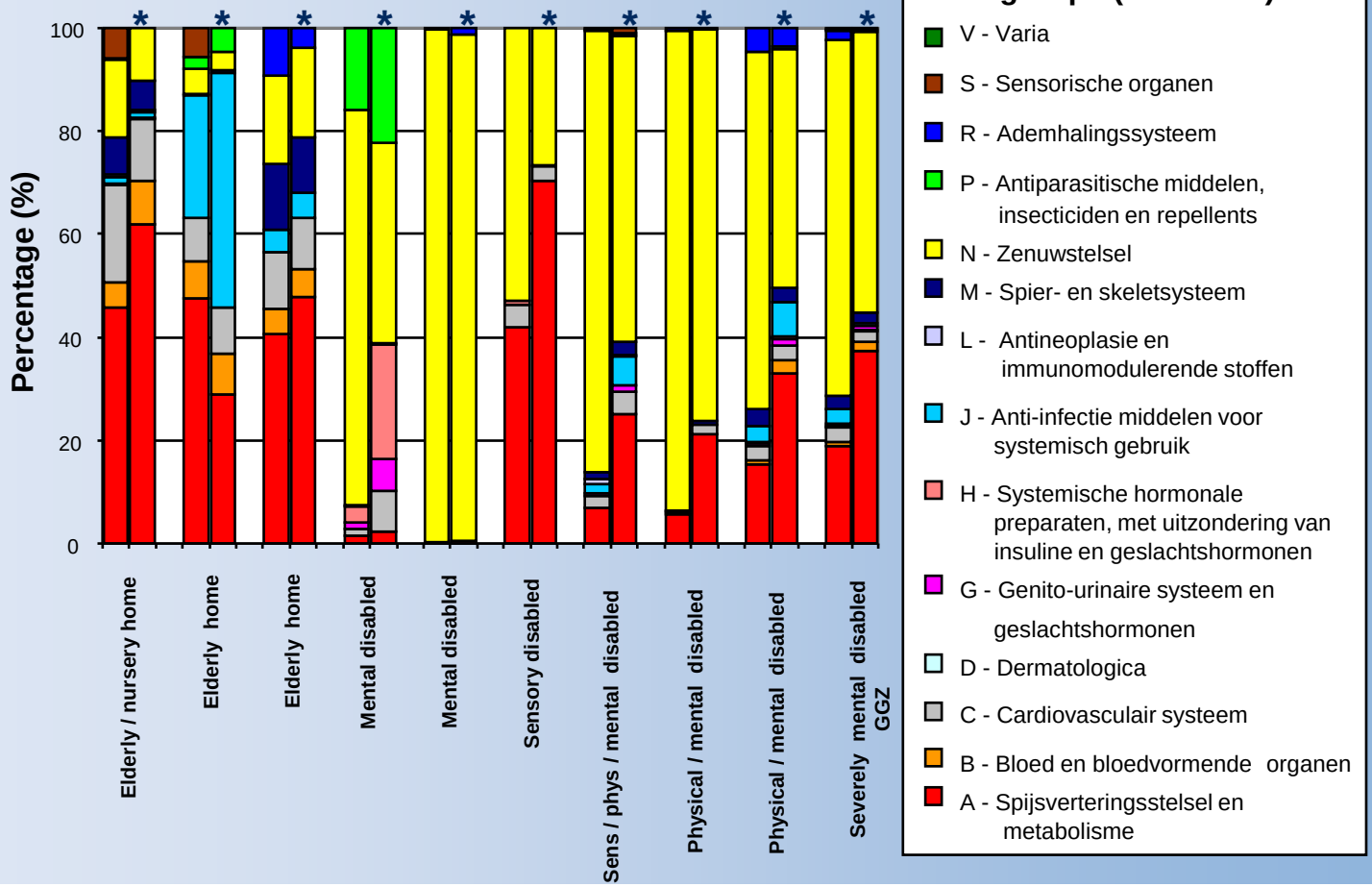
Total load per year with and without excretion (*) as percentage (%)



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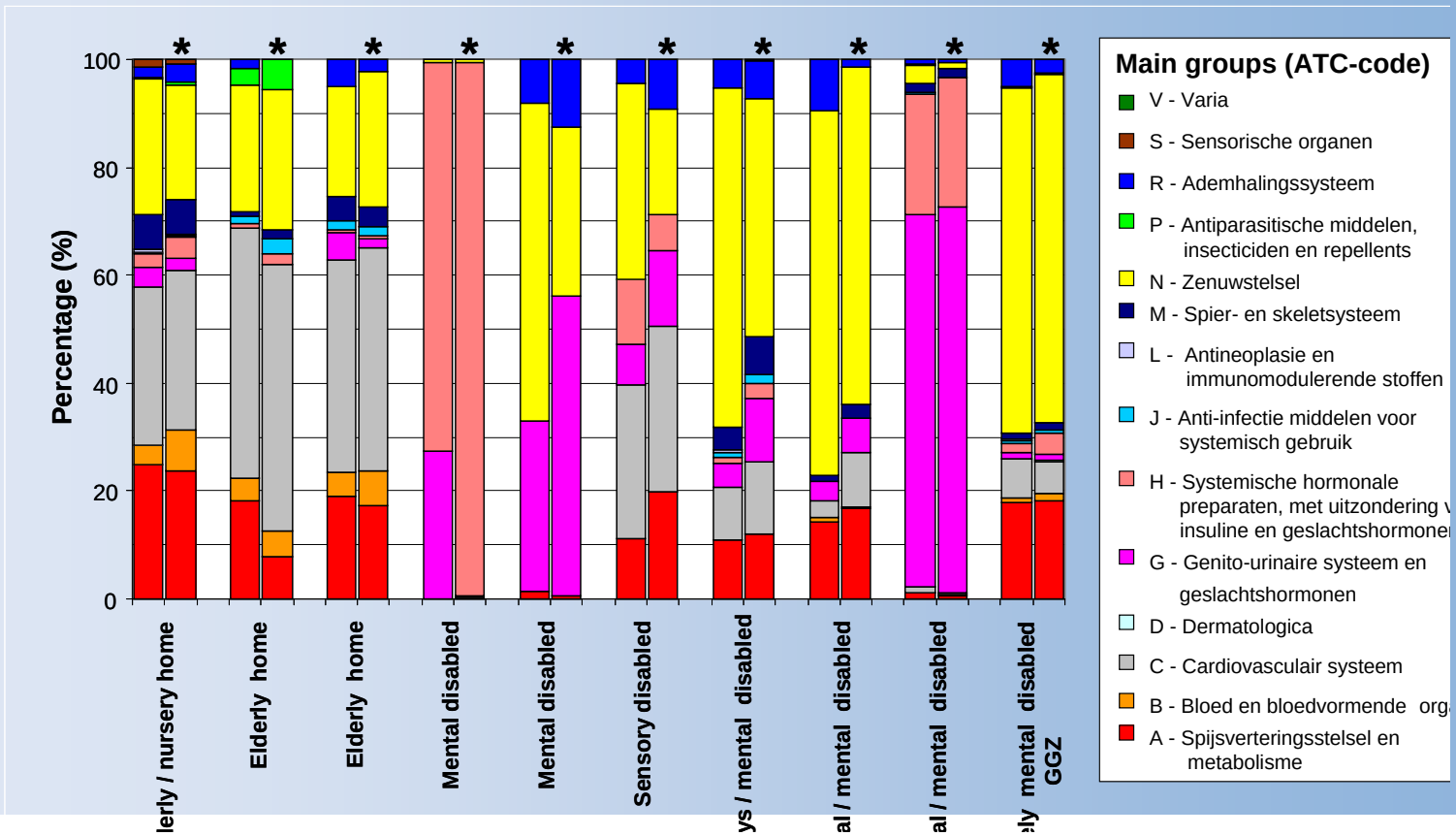
Environmental risk-index: load / DDD
with and without excretion (*)



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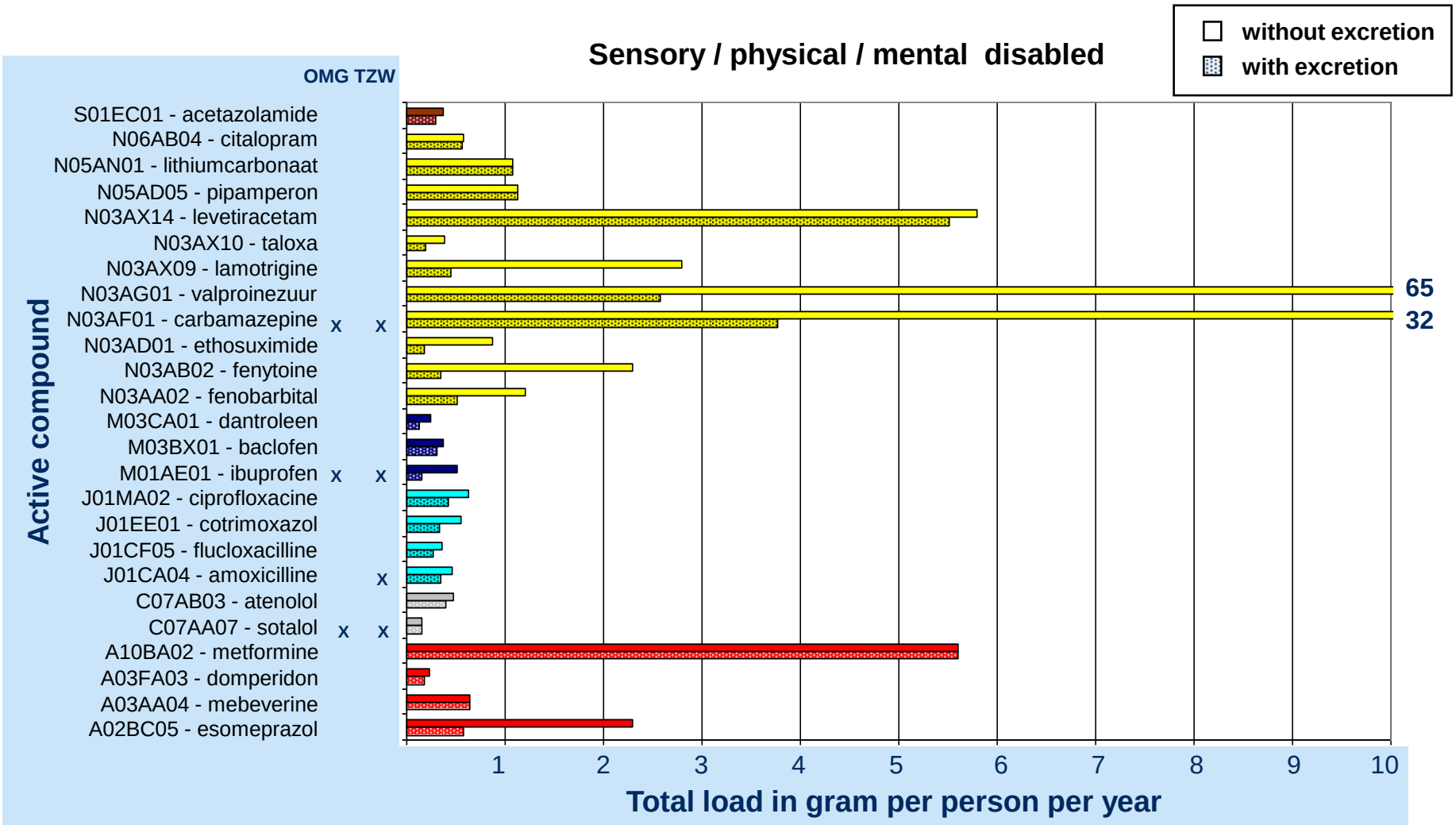
Top 90% of prescribed individual active compounds



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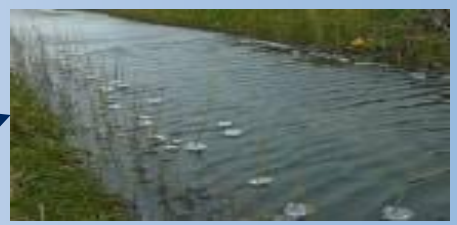
Sample locations: participation 7 different waterboards

Care institution

Households

WWTP



Surface water

- De Dommel
- Aa en Maas
- Zeeuwse Eilanden
- Vallei & Eem
- Hunze en Aas
- Rivierenland
- Roer en Overmaas

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Questions

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