

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

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# Pharmaceuticals and environment: lots of attention!

Ook geneesmiddelen vinden hun weg naar de kraan

**'Perceptie belangrijker dan risicoberekeningen'**

## Prozac bij de vis

**Slootwater medicijncocktail**  
Vrijdag 27 Februari 2004

**KORT NIEUWS**  
**Apotheek te water**

**Zorgen over medicijnresten in water**

**Verbazing over uitspraken Van Geel over risicostoffen in drinkwater**

**Gedwongen medicatie?**

**VRON-werkgroep evalueert reductie van geneesmiddelen in het watermilieu**

**WINGER AAN DE POELS HOUDEN**

**Geneesmiddelen vervuilen het oppervlaktewater**

Er mag dan weer zalm rond... is het oppervlaktewater allerminst. Hoeveel bestrijdingsmiddelen en hormonen en geneesmiddelen vinden hun weg naar ons drinkwater?

DOOR HENK LEENAERS

**P**enisvorming bij vrouwtjesvulken in de Noordzee, eicellen in het geslacht van mannetjesbrasems, hormoon... is beh...

**V**onder röntgencontrastpilleptica, bèta-blokkers, jodica. Vergelijkbare re... de Staten, Duitsland en... met schreef The Times... ten binnenkort met... sie een omvangrijk... maar de milieusico's van...

**P**lassende patiënten Het geneesmiddelengebruik is explosie... de Tweede Wereldoorlog, toen antibi... ontdekt. Nam in de decennia van de... het medicijngebruik toe door een stijg... vaart en een verbetering van de medi... ningen. In de eenentwintigste eeuw zo... zing voor een verdere consumptiegroe... depressiva, aldus de Amerikaanse Food and...

**G**eneesmiddelen vervuilen het oppervlaktewater. Het is een bekend feit dat geneesmiddelen... worden gebruikt. Maar hoe vaak komen ze... in het oppervlaktewater terecht? En hoe... worden ze afgevoerd? Dit zijn de vragen die... worden gesteld door de Vron-werkgroep...

**V**an onze redacteur DEN HAAG - Drinkwaterwinners hebben het ministerie van VWS gevraagd om geneesmiddelen voortaan te toetsen op hun milieueigenschappen. De sector maakt zich zorgen over de vervuiling van met name oppervlaktewater met de resten van medicijnen.

**O**nderzoeken die vorig jaar zijn uitgevoerd door de waterkwaliteitsmetende RIZA en KIWA hebben duidelijk gemaakt dat geneesmiddelen in het oppervlaktewater zijn te vinden. Het is vooral de aanwezigheid van antibiotica, pijnkillers en hormonen die zorgen voor problemen. Volgens de Vron-werkgroep, die bestaat uit vertegenwoordigers van de watersector, de gezondheidssector en de milieusector, is de aanwezigheid van geneesmiddelen in het oppervlaktewater een ernstig probleem. Het is vooral de aanwezigheid van antibiotica, pijnkillers en hormonen die zorgen voor problemen. Volgens de Vron-werkgroep, die bestaat uit vertegenwoordigers van de watersector, de gezondheidssector en de milieusector, is de aanwezigheid van geneesmiddelen in het oppervlaktewater een ernstig probleem.

**V**erder zou er al... zijn als zore... her uit... de drinkwatersector, is een tand... gemodifice... dering kun... je VEWIN da... ellen.

**W**aterpijp heeft de der tijd flink op kos... CB's, bacteriën en vi... plosmiddelen, bestrij...

**R**uim driekwart van de antibiotica in het afvalwater komt ongehinderd in sloten en beken terecht'

**V**erwijde brasems De nu in het oppervlaktewater gemeten geneesmid...

**V**oor geneesmiddelen bestaan nog geen drinkwaternormen. Als er al iets wordt gemeten, gaat het om een sportieve van enkele miljardsten grammen per liter. Drink je van dat water je leven lang dagelijks twee li...

# 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
- $\beta$ -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, Spatial 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

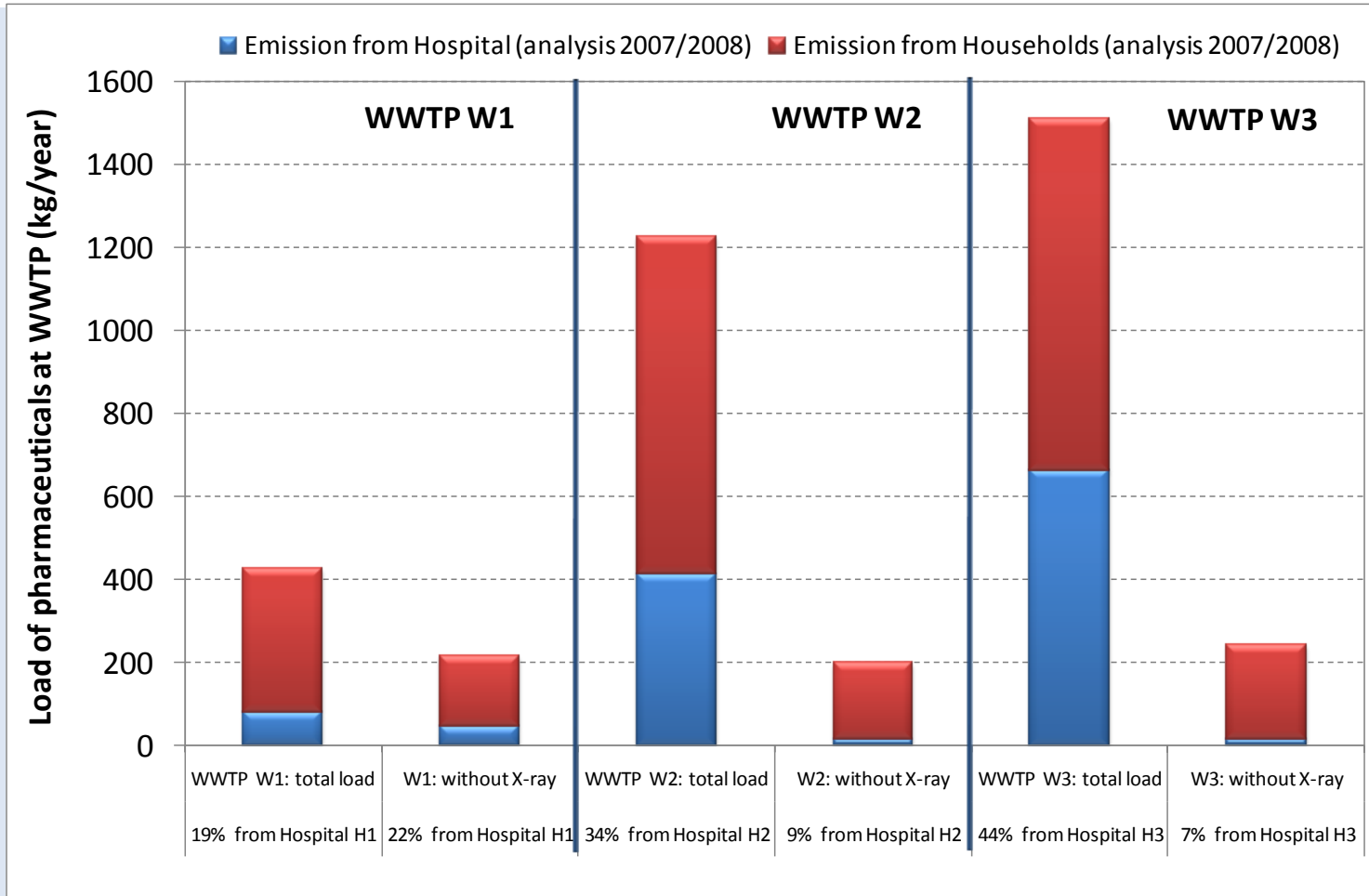
– Uitvoeren van haalbaarheidstudie en pilots naar emissiereducerende maatregelen in ziekenhuizen en zorginstellingen.

# 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





# 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 households  
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:

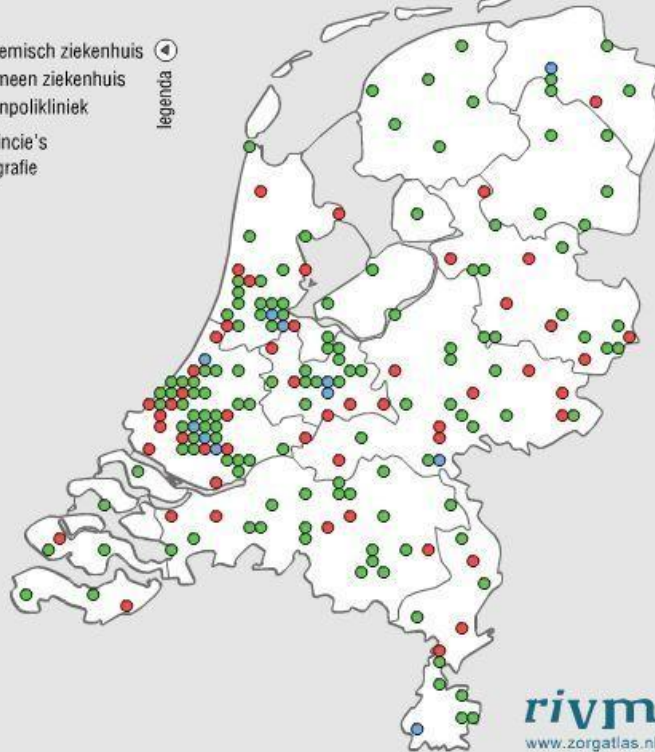
- Home for the elderly
- Nursery homes
- Physical disabled
- Mental disabled
- Sensory disabled
- Severely mental disabled (GGZ)
- Care institutions for addictions

# Hospitals and nursing/elderly homes in The Netherlands

## Locaties ziekenhuizen juli 2008

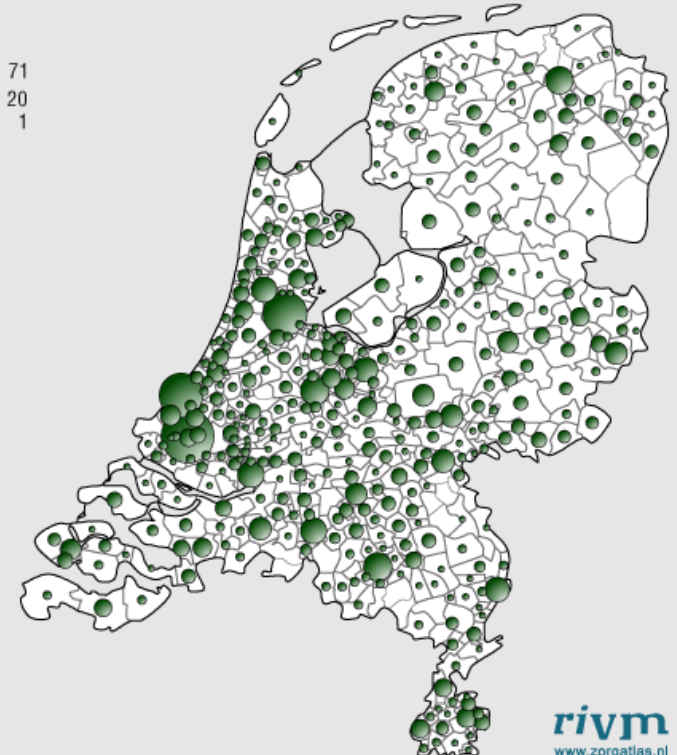
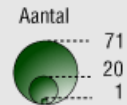
Academische en algemene ziekenhuizen inclusief buitenpoliklinieken

- Academisch ziekenhuis
- Algemeen ziekenhuis
- Buitenpolikliniek
- Provincie's
- Topografie



## Aantal verpleeg- en verzorgingshuizen 2007

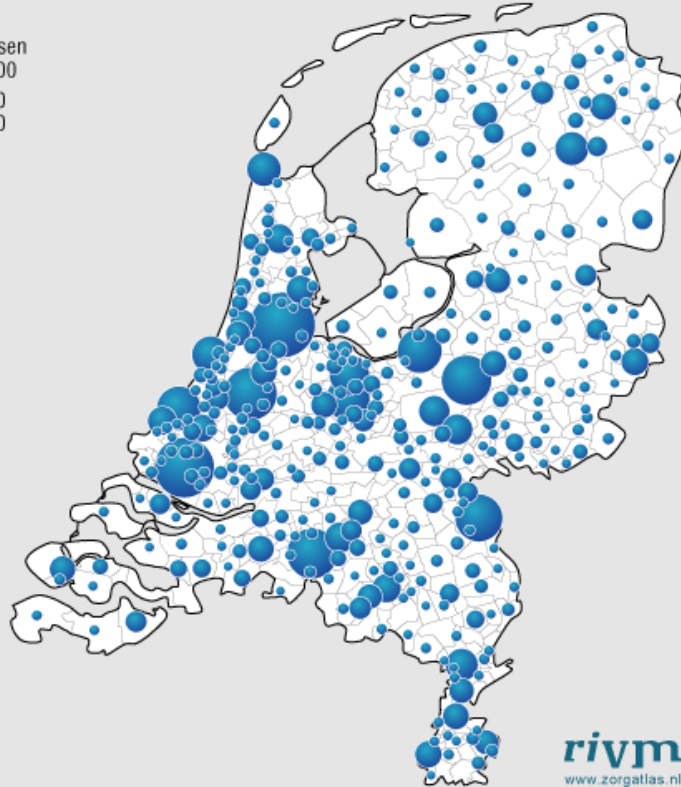
per gemeente



# Mental and physical disabled in The Netherlands

Verstandelijk gehandicapten wonen 2003  
per gemeente

Aantal plaatsen  
1500  
700  
100



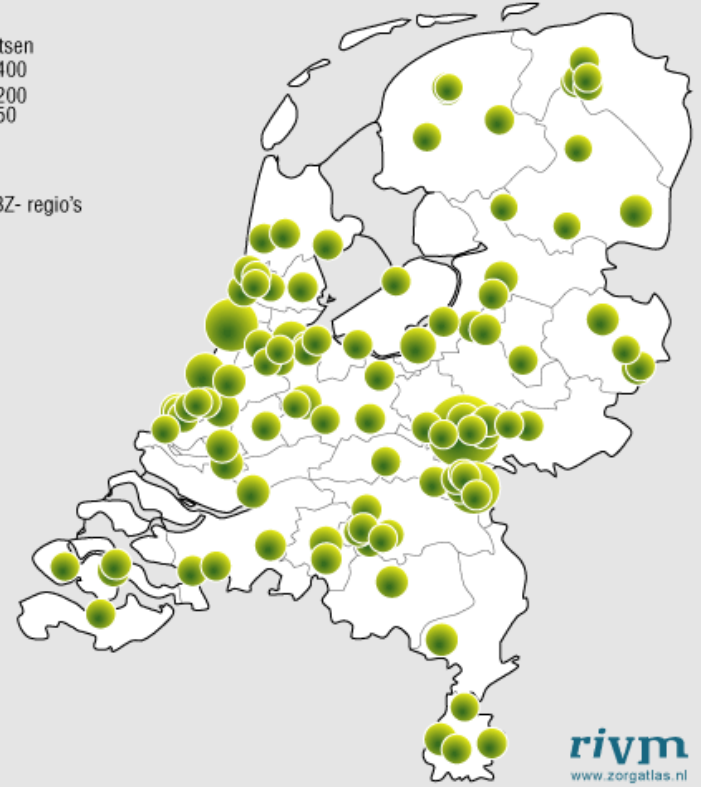
Bron: VWS

**rivm**  
www.zorgatlas.nl

Lichamelijk gehandicapten wonen 2003  
locaties en capaciteiten

Aantal plaatsen  
400  
200  
50

— AWBZ- regio's

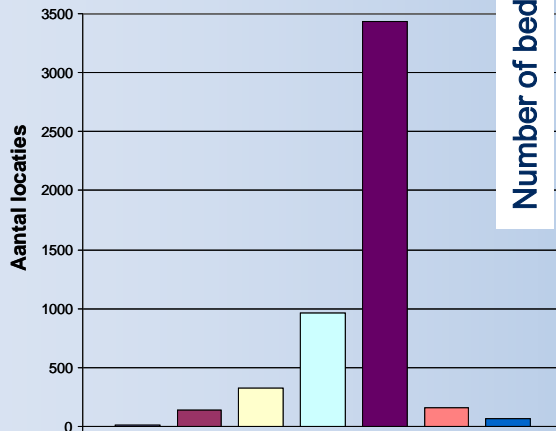


Bron: VWS

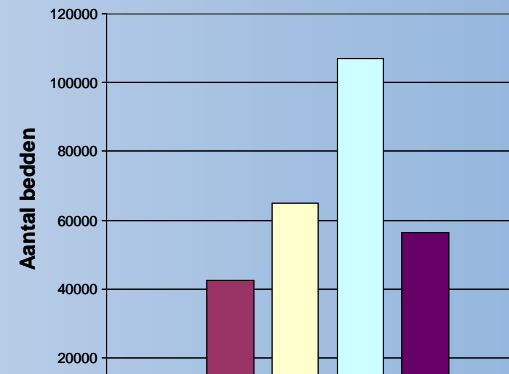
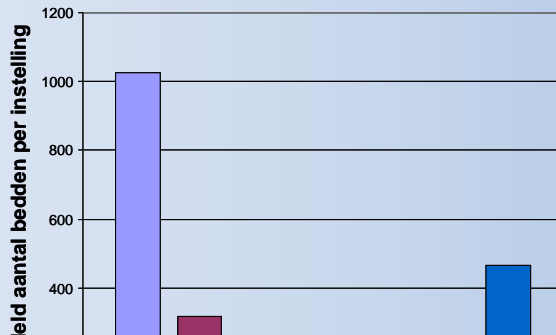
**rivm**  
www.zorgatlas.nl

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

Number of locations

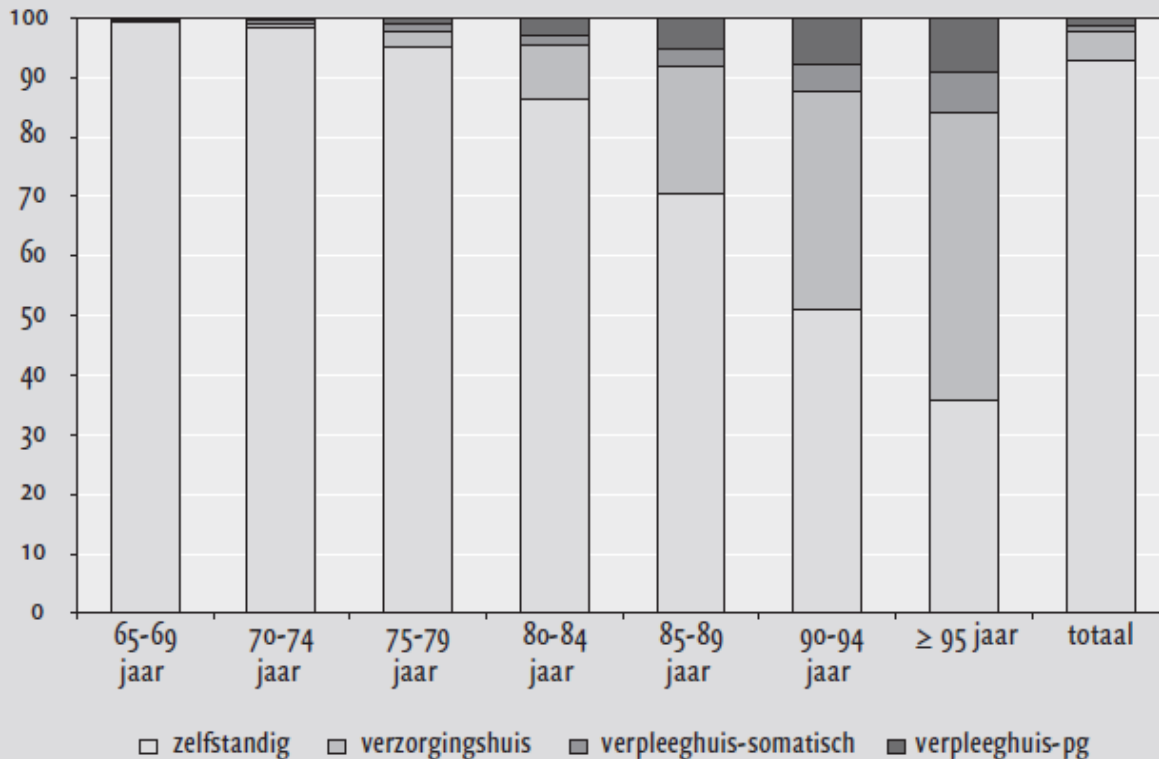


Number of beds per location



- Academic hospital
- Common hospital
- Home for the elderly
- Nursery home
- Mental disabled
- Physical disabled
- Severely mental disabled (GGZ)

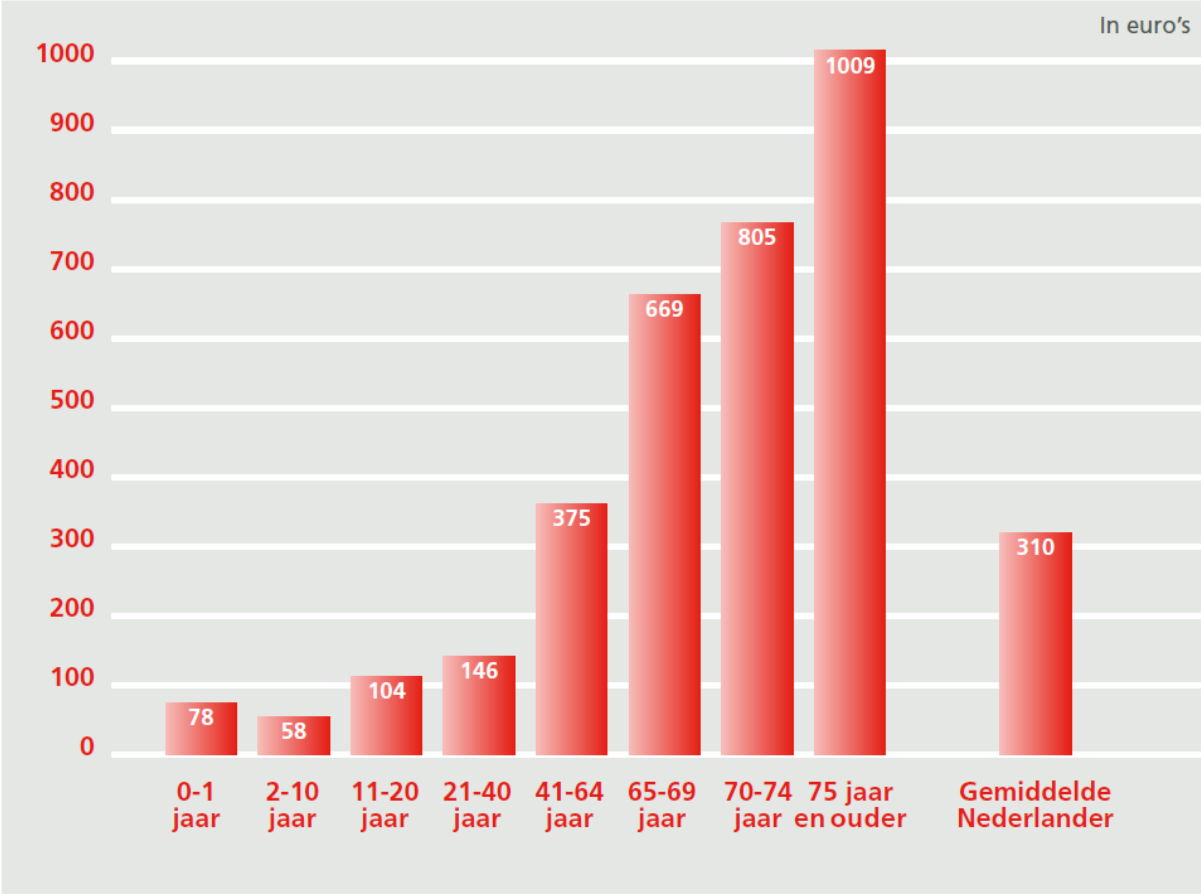
# How do people live?



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

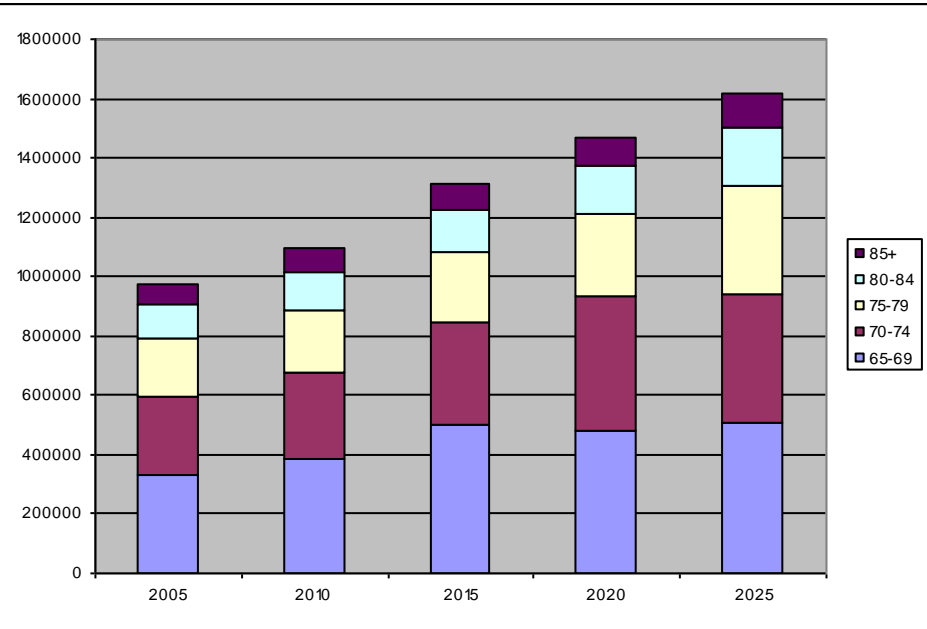


# Intake pharmaceuticals by age



Bron: Stichting Farmaceutische Kengetallen

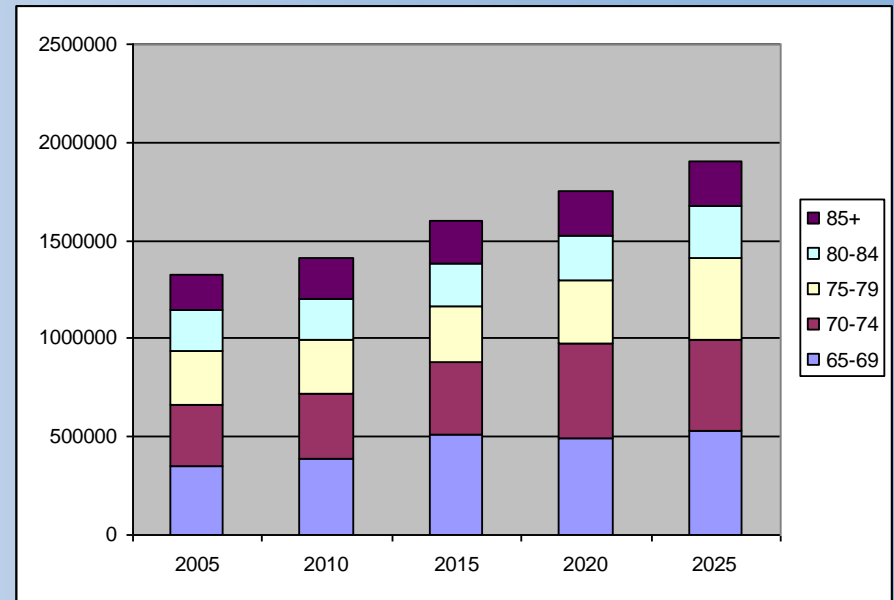
# Demographic trends >65 jaar



1.6 million males in 2025

**Increased use  
pharmaceuticals expected!**

1.9 million females in 2025



# 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 bruis tablet 600 mg	2,00 bruis tabletten
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 (besilfaat)	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	6,00 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

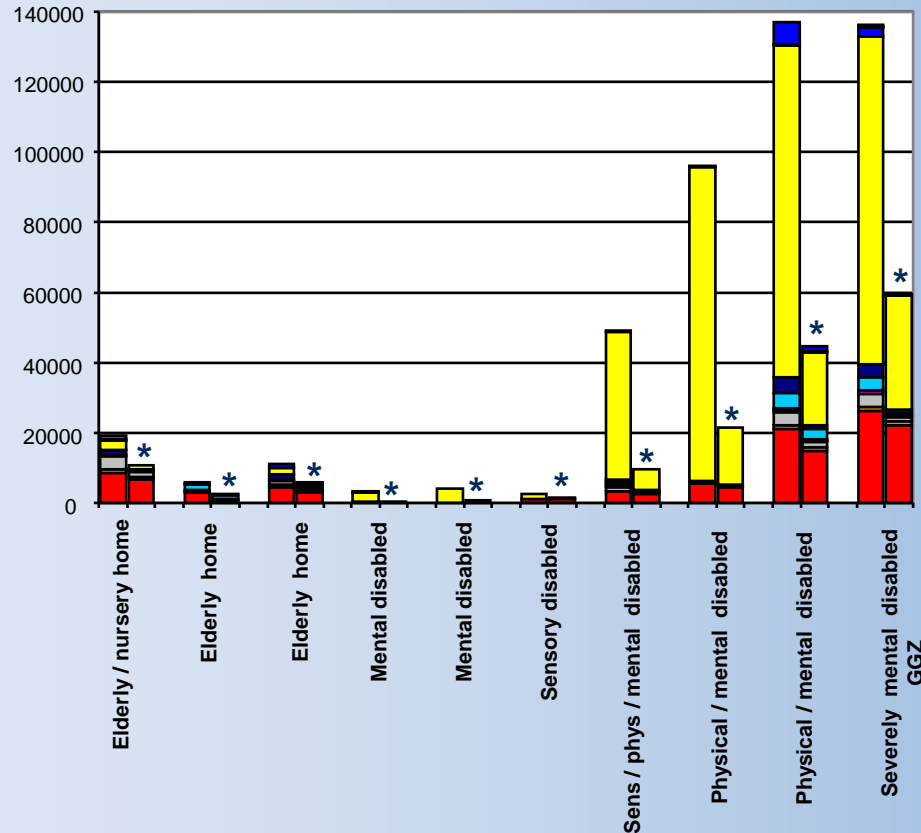
# Approached care institutions: 10

	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

# Establishment database excretion factors for 367 compounds

Active Compound	ATC Code	DDD range (mg) Martindale Drug Reference	DDD mean (mg)	Martindale Drug Reference	DIAM2 database	TU-Harburg database	Unchanged in urine	Unchanged in faeces	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.	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	4-45	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	bioavailability about 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. 15 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	20-150	90	Almost 80% of an oral dose is eliminated as metabolites in the urine, the remainder in the faeces.					1
<b>Fexium (zie Esomeprazole)</b>	<b>A02BC05</b>								<b>1</b>
Mebeverine	A03AA04	150-400	275	Mebeverine is completely metabolised by hydrolysis to veratric acid and mebeverine alcohol, the latter of which may then be conjugated. The metabolites are excreted in the urine.	Excreted in urine.				1
Dimeticono/Simeticone	A03AX13	300-1000	650		Excreted as unchanged drug in faeces.	0			1
Scopolaminebutylhyoscyne 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.	90% 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				

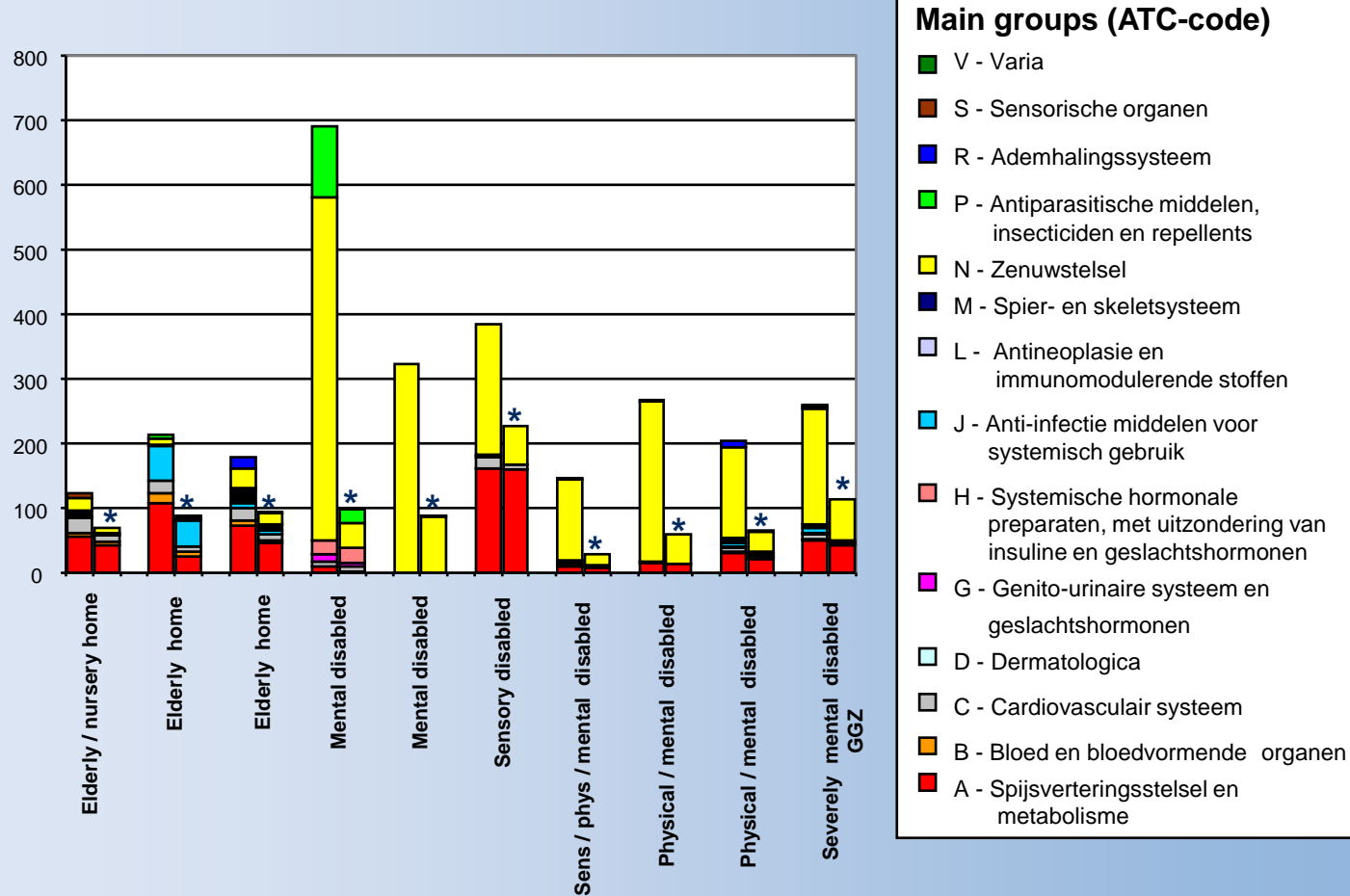
# Total load in gram per year with and without excretion (\*)



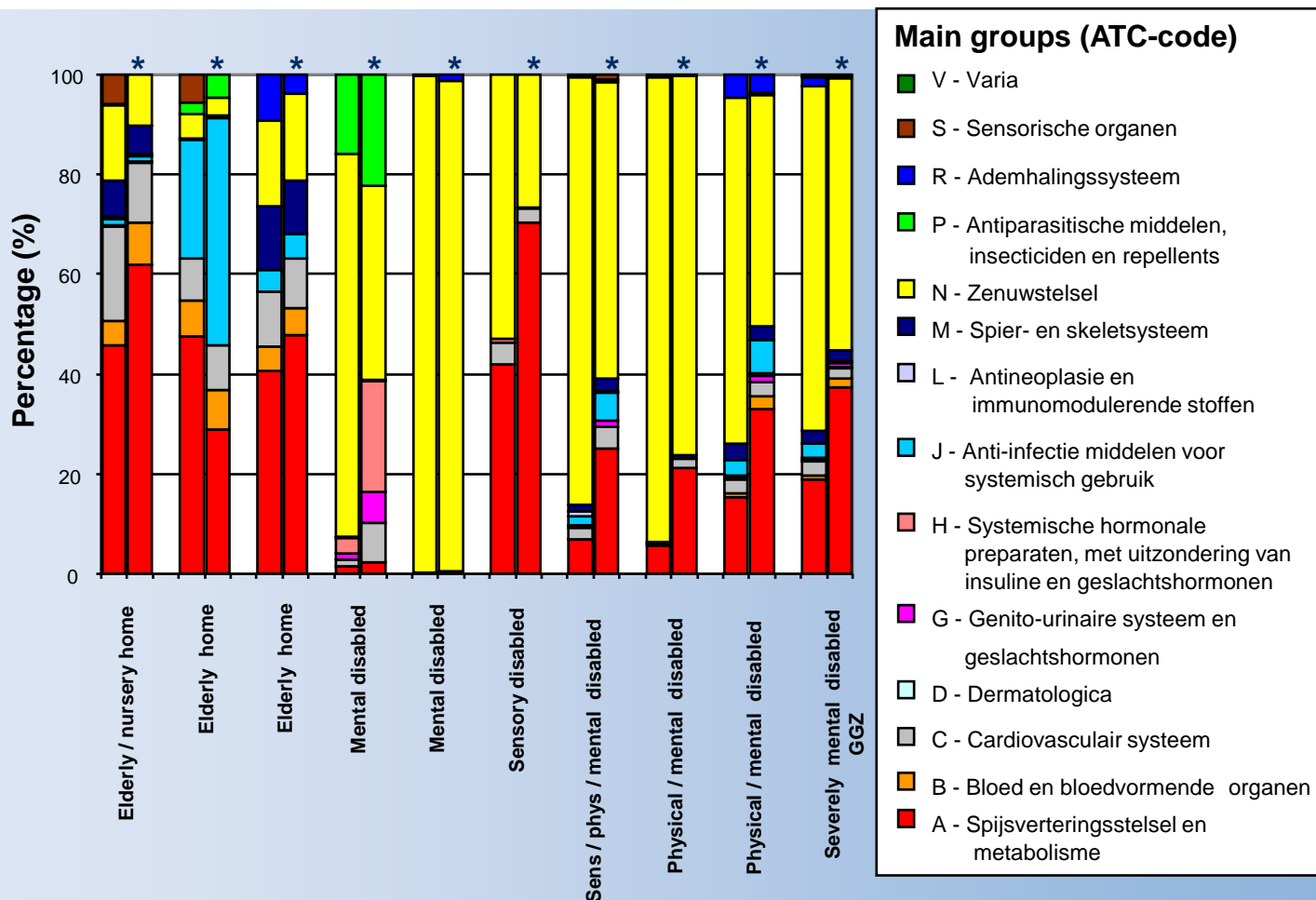
## Main groups (ATC-code)

- V - Varia
- S - Sensorische organen
- R - Ademhalingsstelsel
- P - Antiparasitische middelen, insecticiden en repellents
- N - Zenuwstelsel
- M - Spier- en skeletstelsel
- L - Antineoplasie en immunomodulerende stoffen
- J - Anti-infectie middelen voor systemisch gebruik
- H - Systemische hormonale preparaten, met uitzondering van insuline en geslachtshormonen
- G - Genito-urinaire systeem en geslachtshormonen
- D - Dermatologica
- C - Cardiovasculair systeem
- B - Bloed en bloedvormende organen
- A - Spijsverteringsstelsel en metabolisme

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

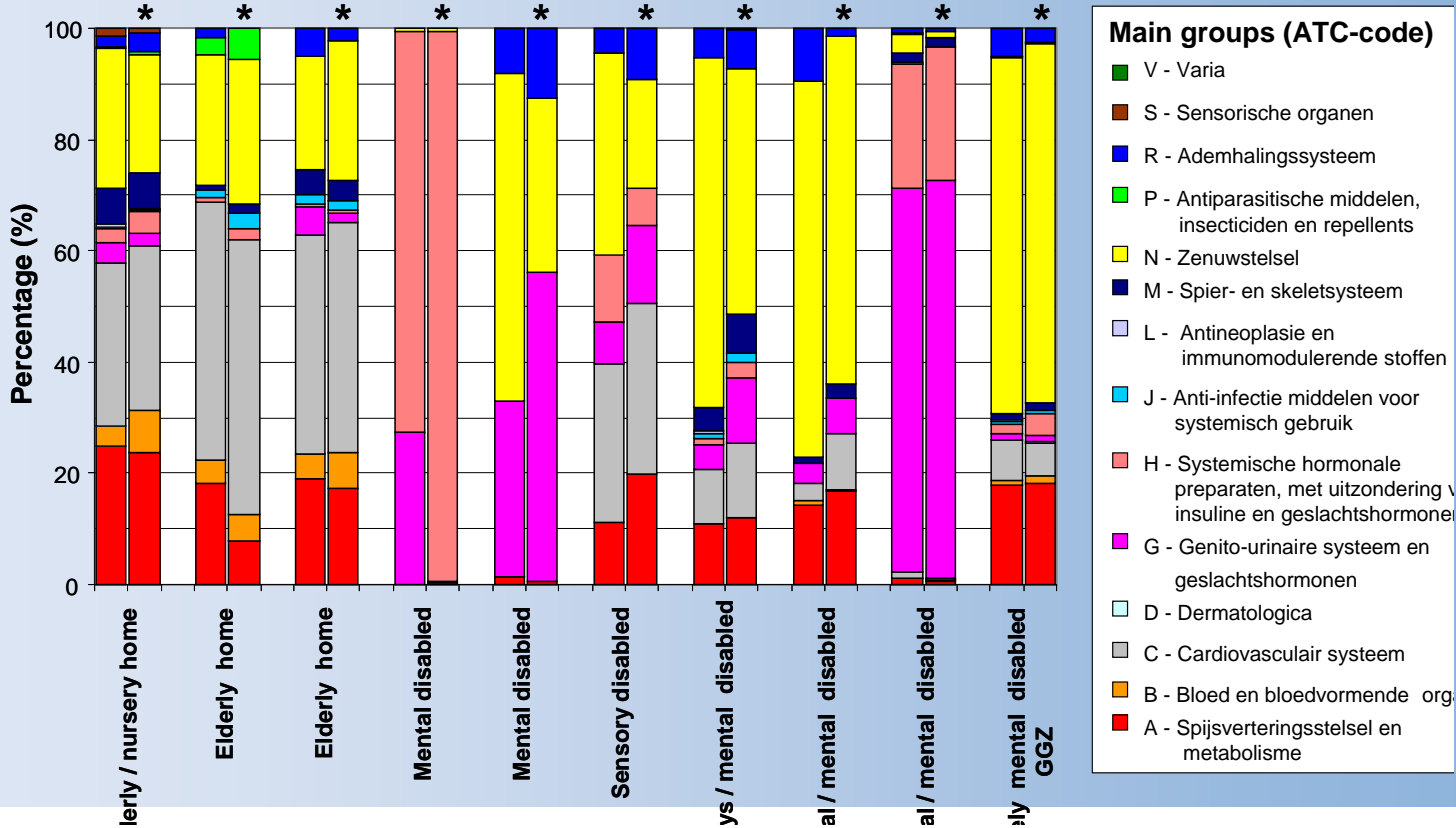


# Total load per year with and without excretion (\*) as percentage (%)

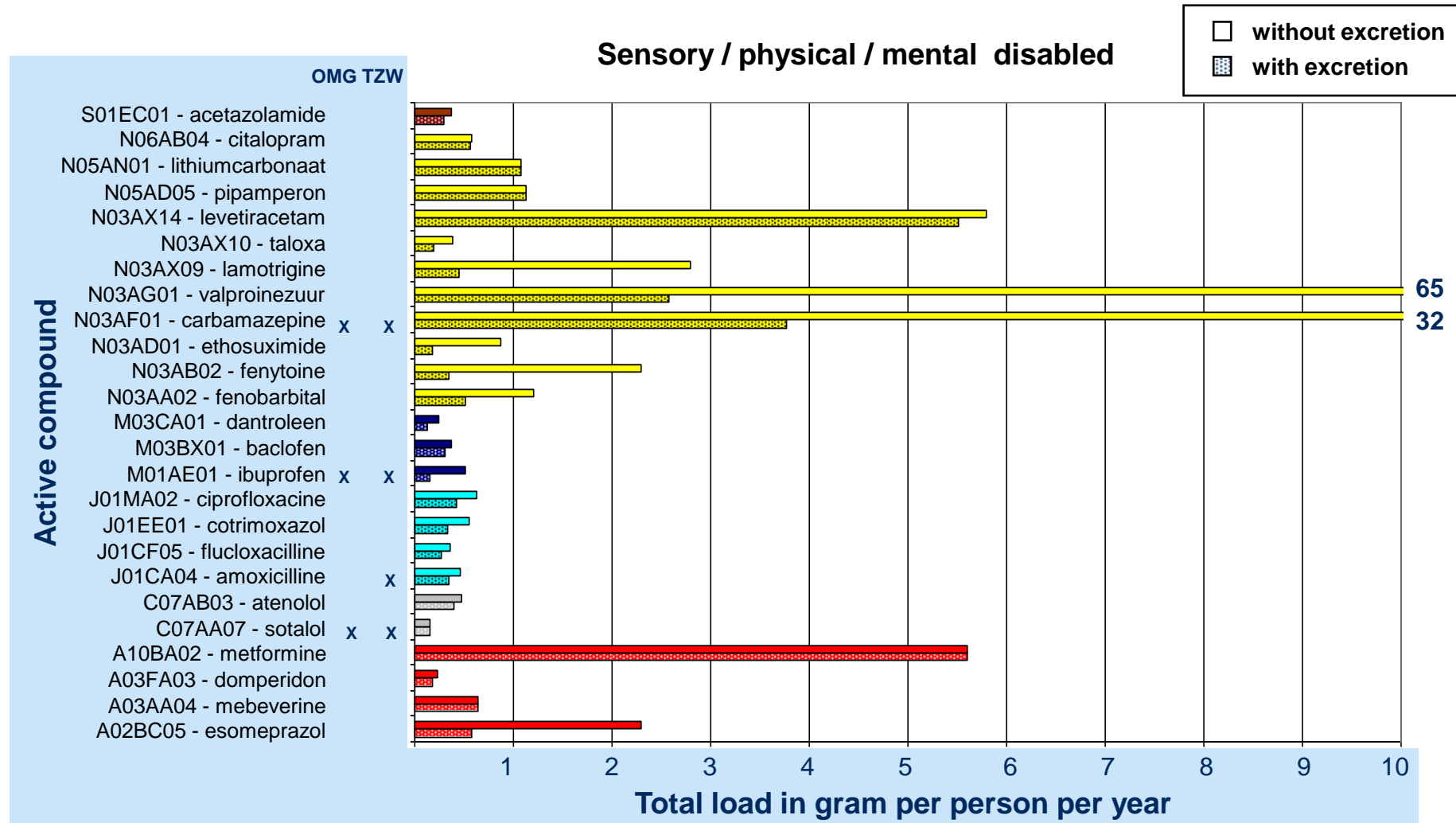




# Environmental risk-index: load / DDD with and without excretion (\*)



# Top 90% of prescribed individual active compounds



# Sample locations: participation 7 different waterboards

Care institution



Households



X

X

X

WWTP



X

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



Surface water

# Questions

?