MORPHEUS
Model Areas for Removal of Pharmaceutical Substances in the South Baltic

Universität Rostock
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EUROPEAN UNION
European Regional Development Fund

WP3 – Regional Consumption Patterns of Pharmaceuticals

PP3
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(University of Rostock)

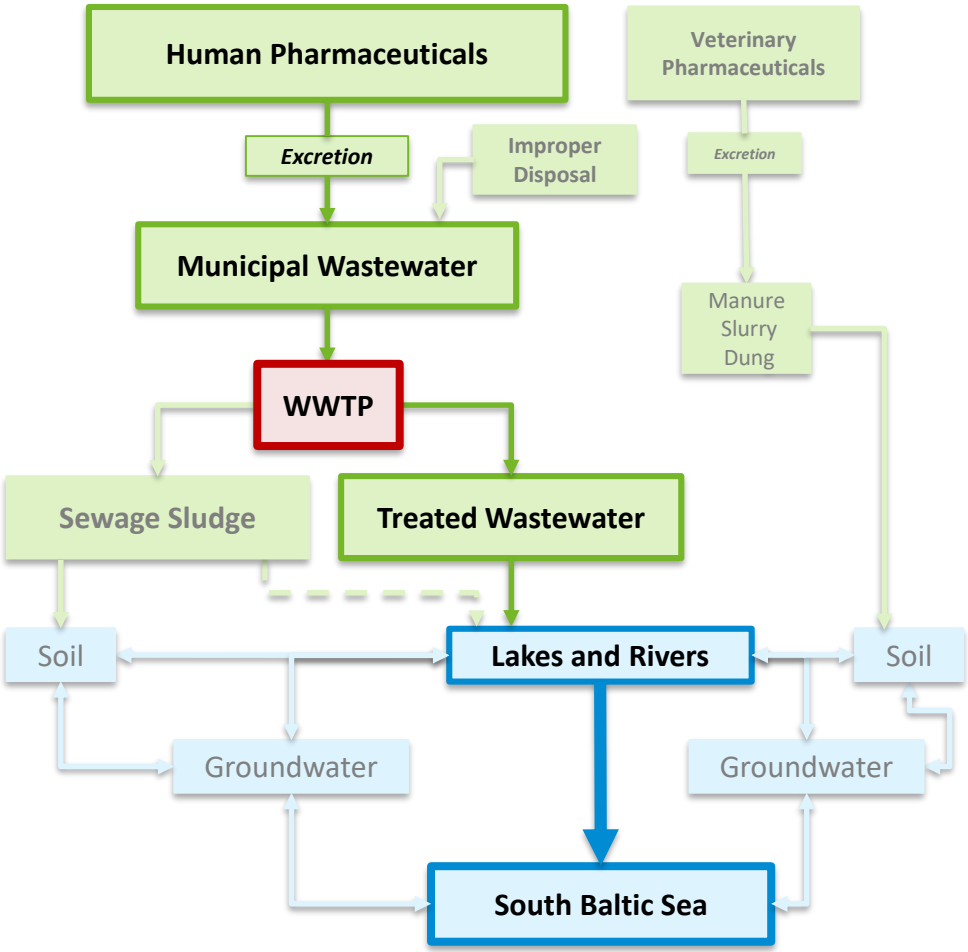
Agenda

- Boundary Conditions for Consumption Analysis
- Regional Data Availability
- Model Approaches
- Results: Country-wise & Comparison
- Conclusion
- Q & A

Consumption Analysis

Assumptions

- Top-down approach
- Main path of pharmaceuticals into environment via WWTPs
- Improper disposal and veterinary application is not quantifiable so far
- Total intake loads of pharmaceuticals calculated by “average inhabitants”
- Sludge not regarded yet



Reduced list of representative Pharmaceuticals

Combining criteria from WP3 and WP4

J – Antiinfectives for systemic use

Amoxicillin
Azithromycin
Ciprofloxacin
Clarithromycin
Erythromycin
Sulfamethoxazole

M – Muscolo-skeleton system

Diclofenac
Ibuprofen
Naproxen

N – Nervous system

Paracetamol
Carbamazepine
Oxazepam
Risperidone
Fluoxetine

G – Genito urinary system and sex hormones

Estradiol
Estrone
Ethinylestradiol

C – Cardiovascular system

Atenolol
Metoprolol
Propranolol
Bezafibrate

A – Drugs used in diabetes

Metformin

V – Various

Iopromid

Characterization of Pharmaceuticals

- ATC = anatomical-therapeutic-chemical classification
  - Case of application (Letter)
  - Therapeutic/pharmacological (digits + letters)
  - chemical substance (digits)

Each pharmaceutical can be coded by numerous ATCs!

Examples

Pharmaceutical	ATC	Description
Diclofenac	D11AX18	Dermatologicals
	M01AB05 M01AB55	Muscolo-skeletal system Antiinflammatory and antirheumatic, non-steroids Acetic acid derivatives and related substances
	M02AA15	Muscolo-skeletal system Topical products for joint and muscular pain Antiinflammatory preparations, non-steroids for topical use
	N02AJ05	Nervous system Analgesics, opioids Opioids in combination with non-opioid analgesics

Pharmaceutical	AT
Carbamazepine	N

Regional Data Availability

Units of Pharmaceuticals

- DDD = daily defined doses → **Sweden & Germany**
  - "Assumed average maintenance dose per day for a drug used for its main indication in adults" (WHOCC 2018)
  - Unit widely applied in consumption statistics
  - ATC/DDD-Index applicable for Conversion of DDD into loads (grams)

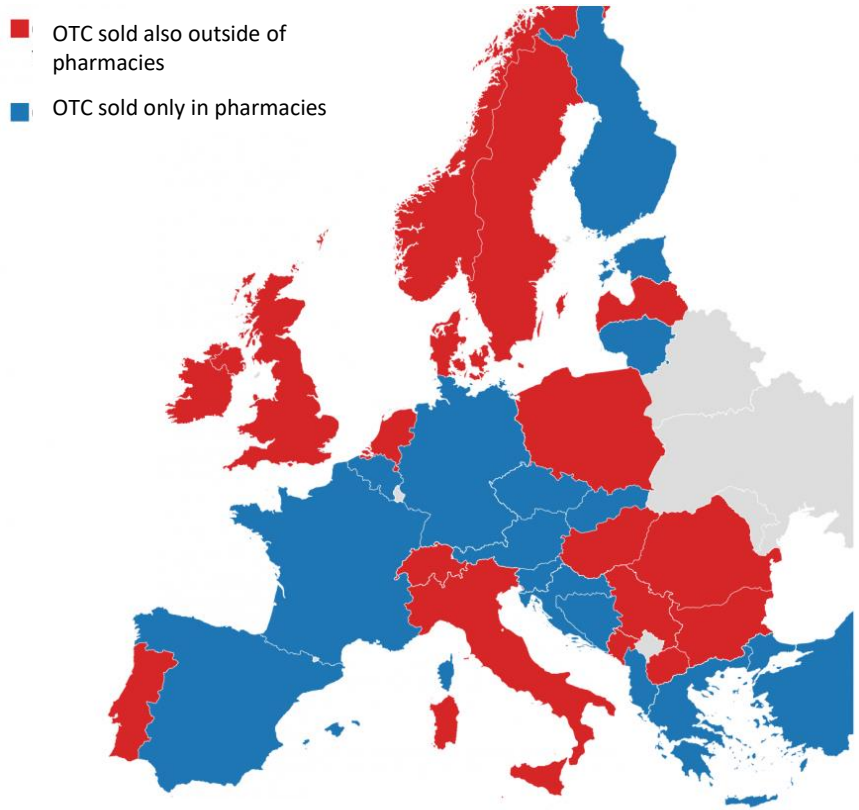
vs.

- EAN codes = trading bar codes of sold products → **Lithuania & Poland**
  - Statistics based on wholesale data
  - Reimbursement of pharmaceuticals by health care funds: recording number of packages
  - Conversion into loads (grams) by package info: number of pills, content

Regional Data Availability

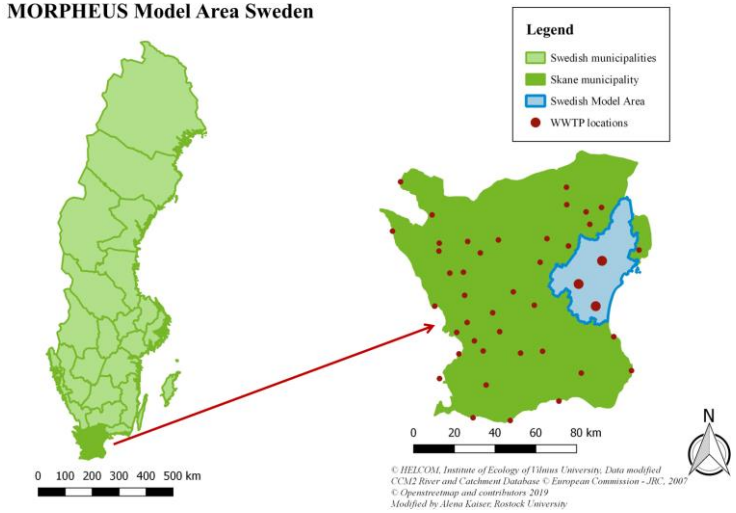
Source and Resolution of Data

- Distribution sites differ: Prescriptions/pharmacies, Application in hospitals or OTC (over the counter sales)
- Data gathered from national authorities, health care institutions and companies
- Differences in
  - Spatial resolution
  - Temporal resolution



Source: DAZ online, 2019

MORPHEUS Model Area Sweden



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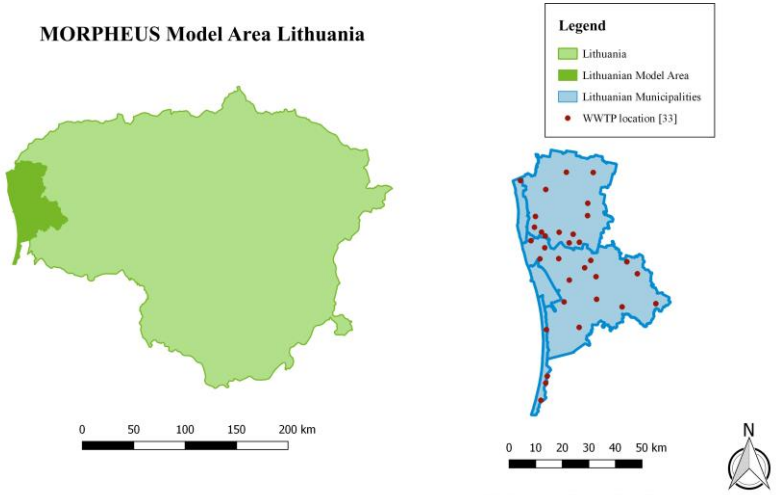
MORPHEUS Model Area Lithuania



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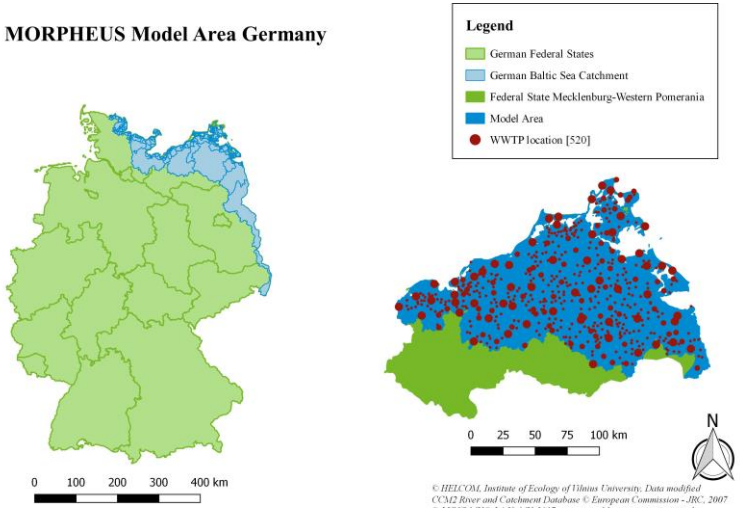
Sergej Suzdalev, Klaipeda University

MORPHEUS Model Area Germany



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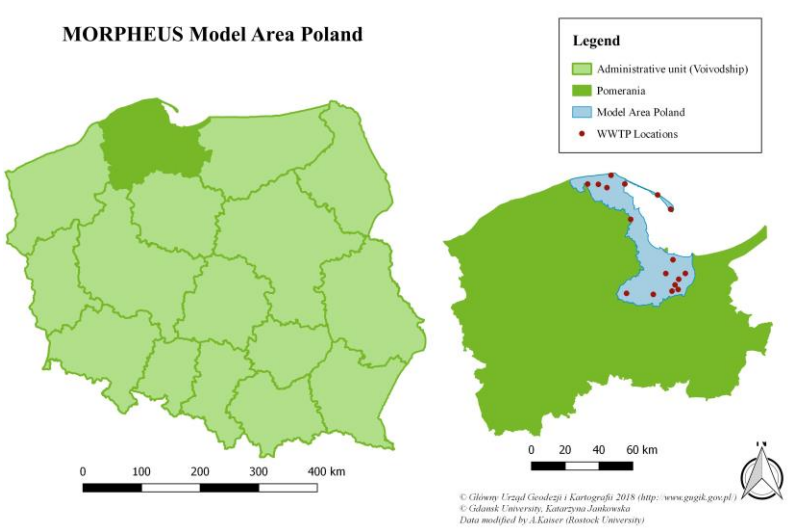
MORPHEUS Model Area Poland



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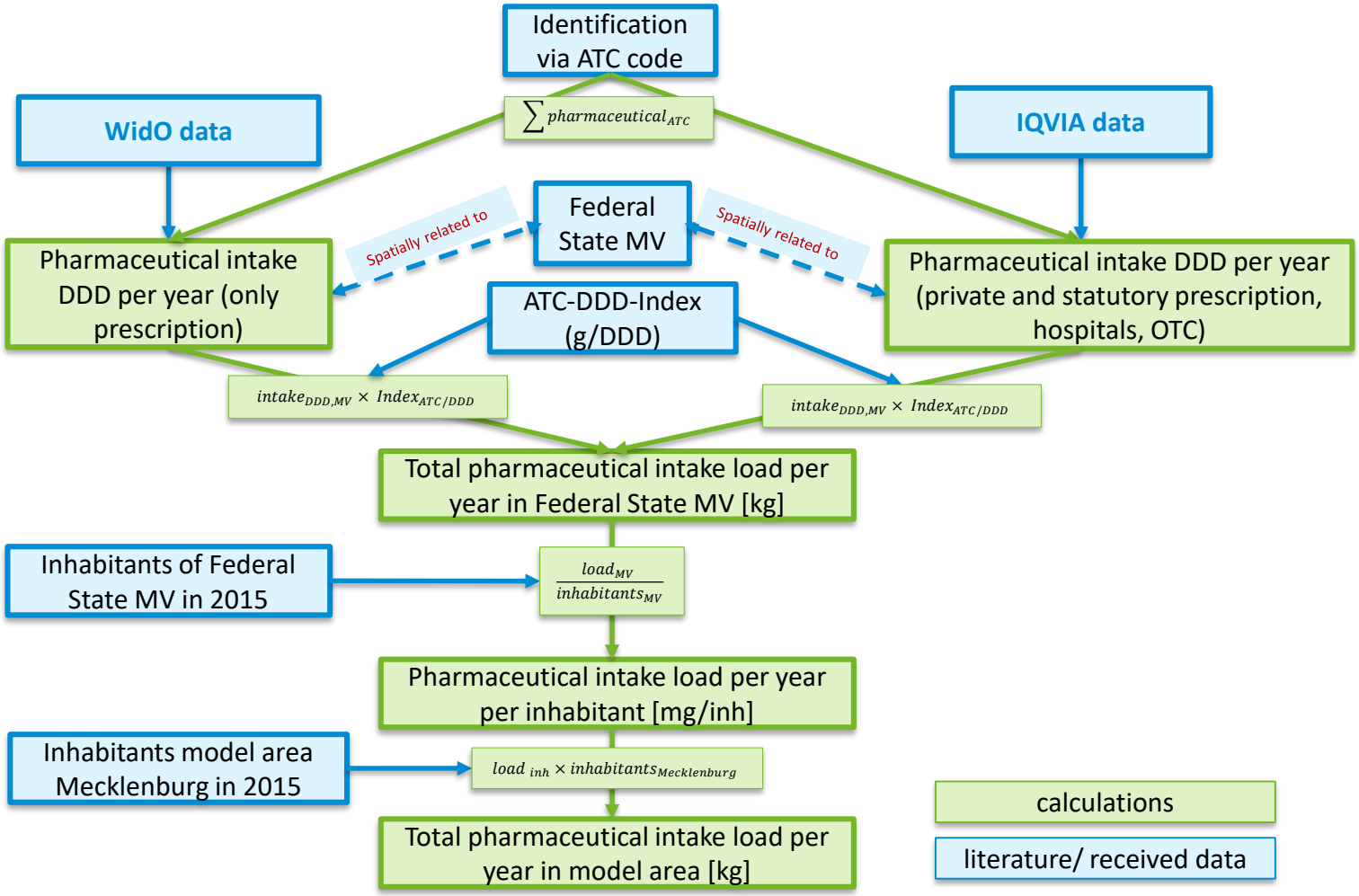
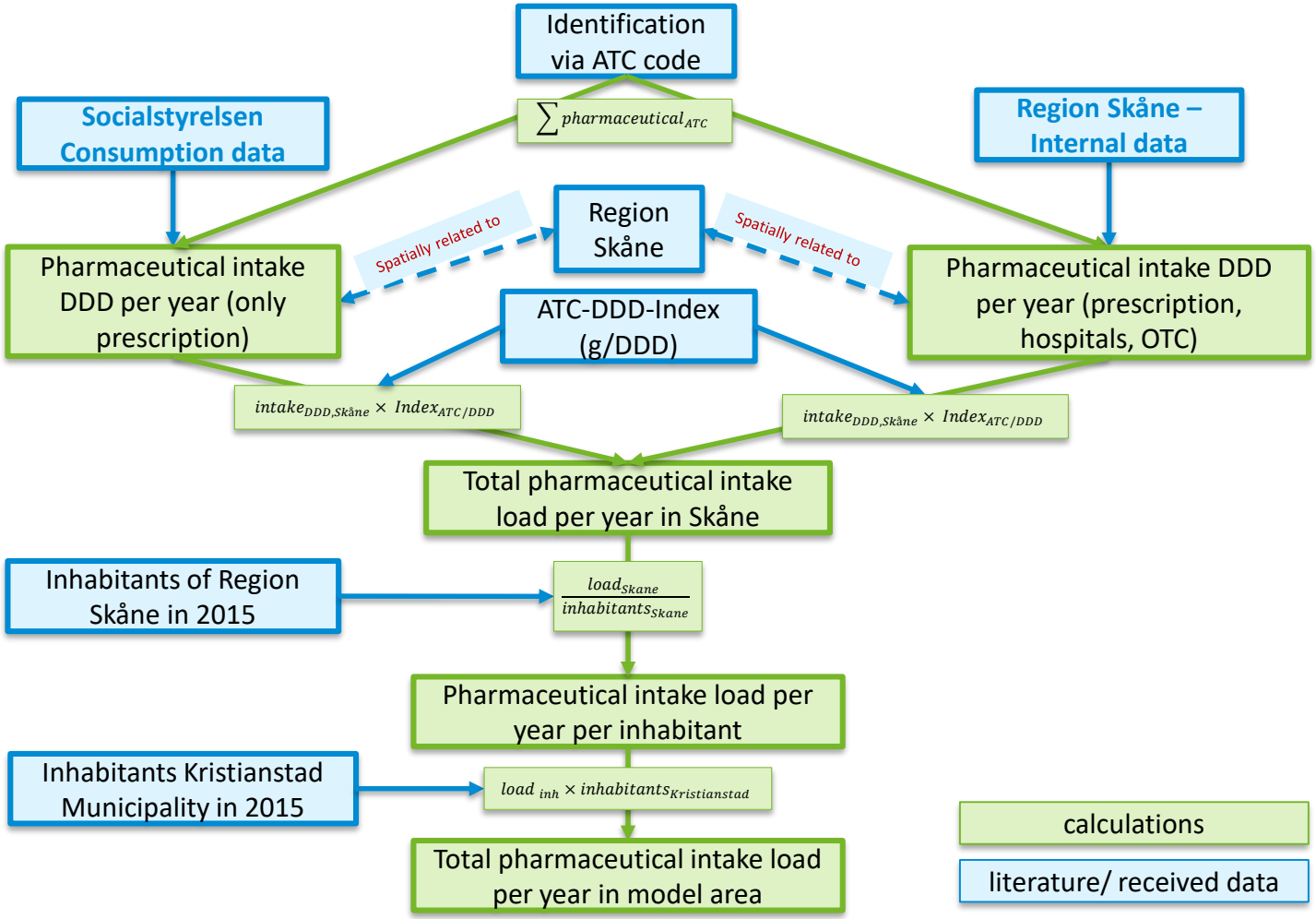
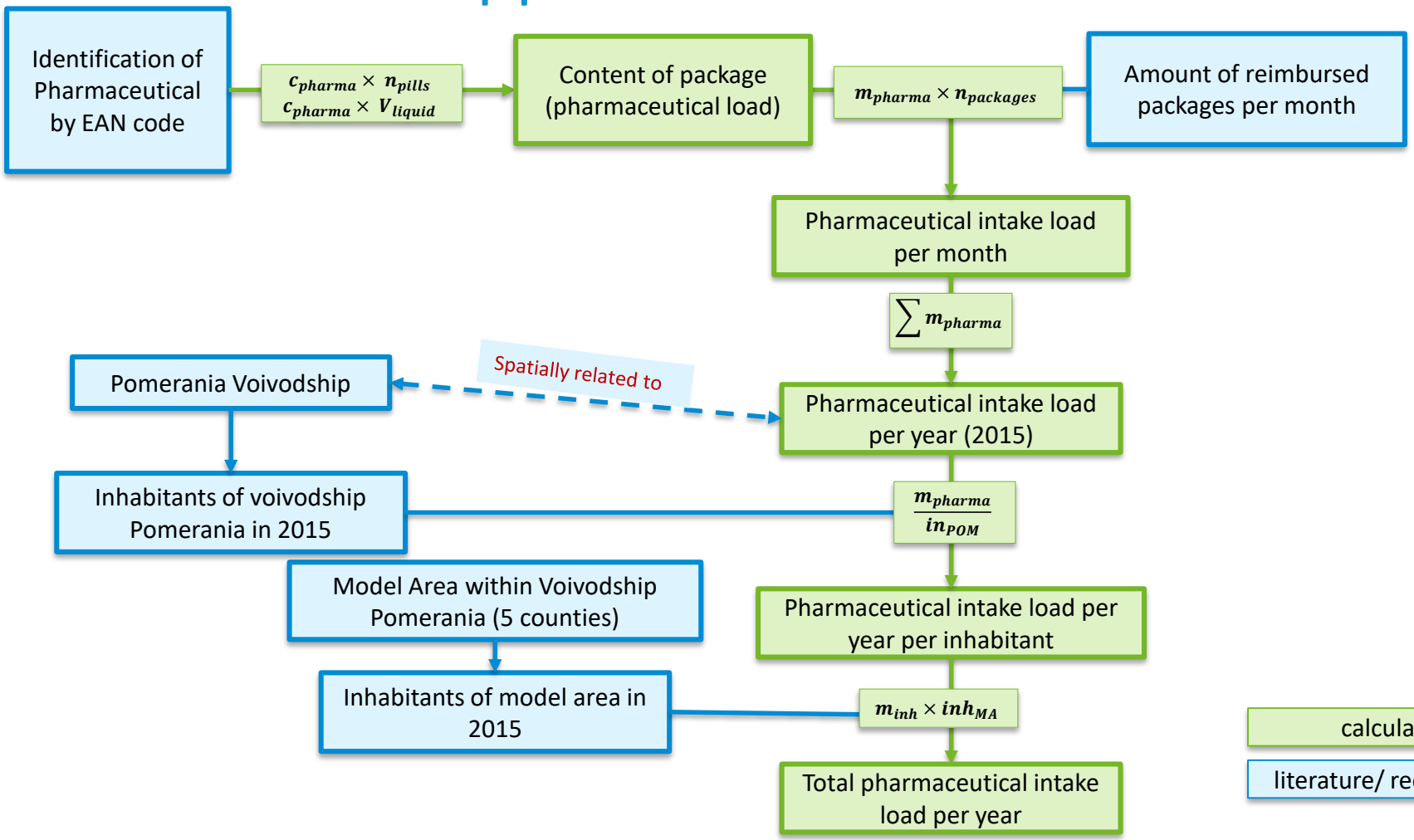
Model Approach GER-Model Area



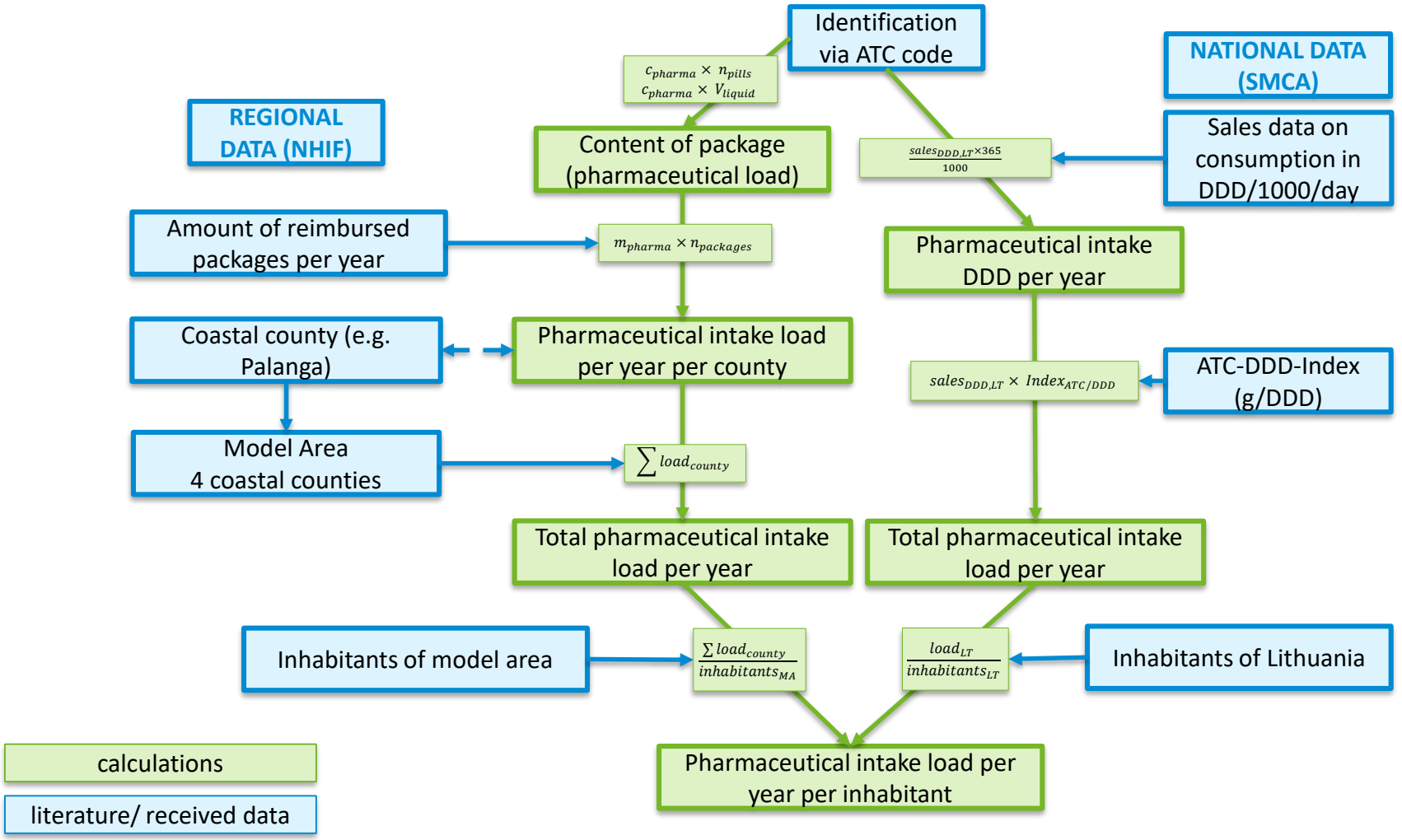
Model Approach SE-model area



Model Approach for PL-model area



Model Approach for LT-model area



Results: country-wise total intake loads

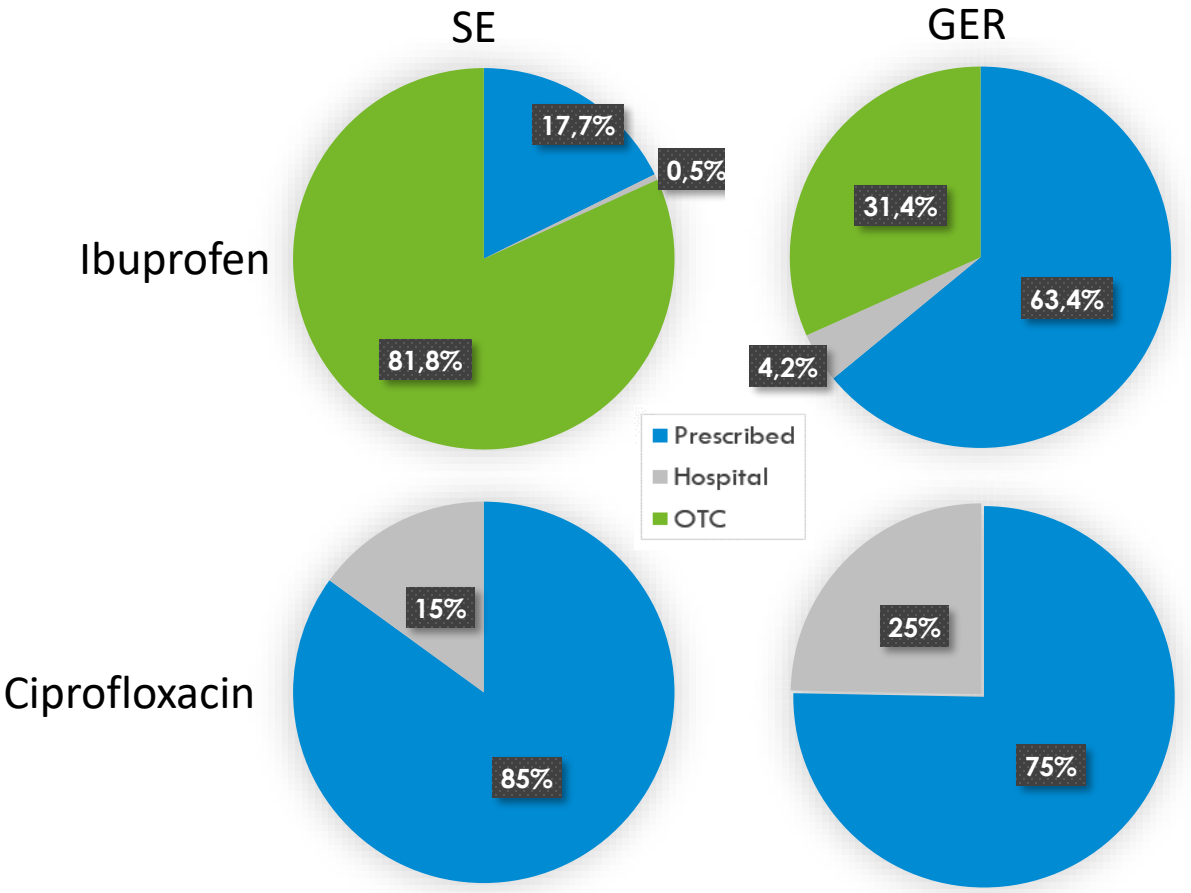
Pharmaceutical	total intake in 2015	Intake per inhabitants
Amoxicillin		
Atenolol		
Azithromycin		
Bezafibrate		
Carbamazepine		
Ciprofloxacin*		
Clarithromycin*		
Diclofenac*		
Erythromycin		
Estradiol		
Ethinylestradiol*		
Fluoxetine		
Ibuprofen*		
Iopromide*		
Metformin		
Metoprolol		
Naproxen*		
Oxazepam*		
Paracetamol*		
Propranolol		
Risperidone		
Sulfamethoxazole*		

Pharmaceutical	N (EAN-codes)	total intake in 2015	Intake per Person
Amoxicillin*			
Atenolol			
Azithromycin			
Carbamazepine			
Ciprofloxacin*			
Clarithromycin			
Diclofenac*			
Erythromycin			
Estradiol			
Fluoxetine			
Ibuprofen*			
Metformin			
Metoprolol			
Naproxen*			
Oxazepam*			
Paracetamol*			
Propanolol			
Risperidon			
Sulfamethoxazole			

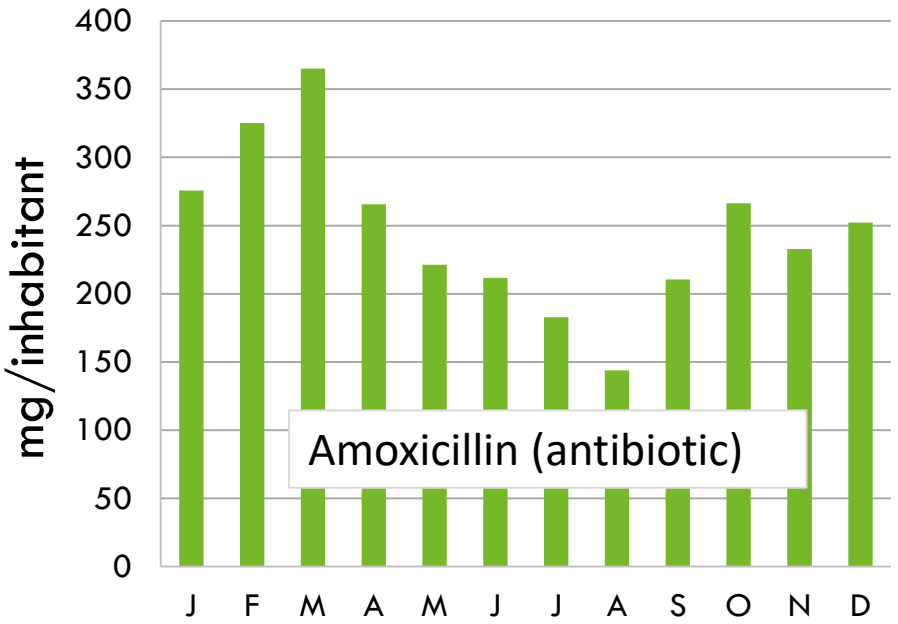
Pharmaceutical	N (EAN-coc	total intake in 2015	Intake per Person
Amoxicillin	63		
Atenolol	2		
Azithromycin	34		
Carbamazepin	11		
Ciprofloxacin	9		
Clarithromycin	32		
Diclofenac	22		
Erythromycin	6		
Estradiol	28		
Ethinylestradiol	8		
Fluoxetin	10		
Ibuprofen	4		
Metformin	22		
Metoprolol	3		
Naproxen	24		
Oxazepam	2		
Propanolol	2		
Risperidon	53		

Pharmaceutical	total intake Kristianstad in 2015 [kg]	Intake per inhabitant in 2015 [mg]
Amoxicillin	34.2	414.7
Atenolol	21.7	262.8
Azithromycin	0.8	9.8
Bezafibrate	2.6	31.4
Carbamazepine	43.5	526.6
Ciprofloxacin	24.6	298.6
Clarithromycin	1.1	13.4
Diclofenac	27.6	334.4
Erythromycin	4.1	50.1
Ethinylestradiol	0.021	0.2
Fluoxetine	3.8	46.0
Ibuprofen	873.4	10585.6
Metformin	1275.5	15459.0
Metoprolol	118.9	1441.2
Naproxen	91.5	1108.6
Oxazepam	5.7	69.6
Paracetamol	4819.9	58416.1
Propranolol	6.3	76.7
Risperidone	0.1	1.4
Sulfamethoxazole	19.7	238.2

Various Distribution Sites of Pharmaceuticals in Sweden and Germany

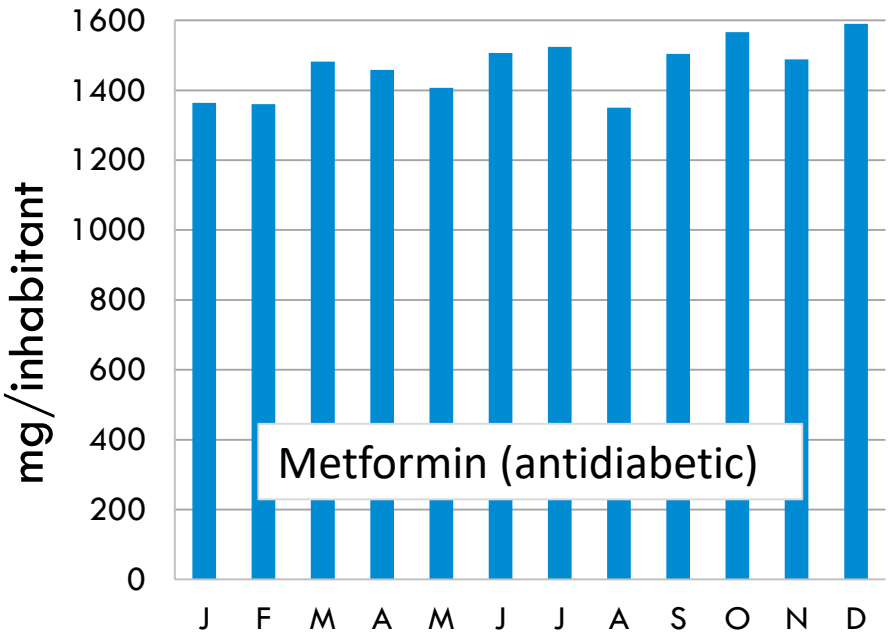


Results: Temporal Resolution in Poland

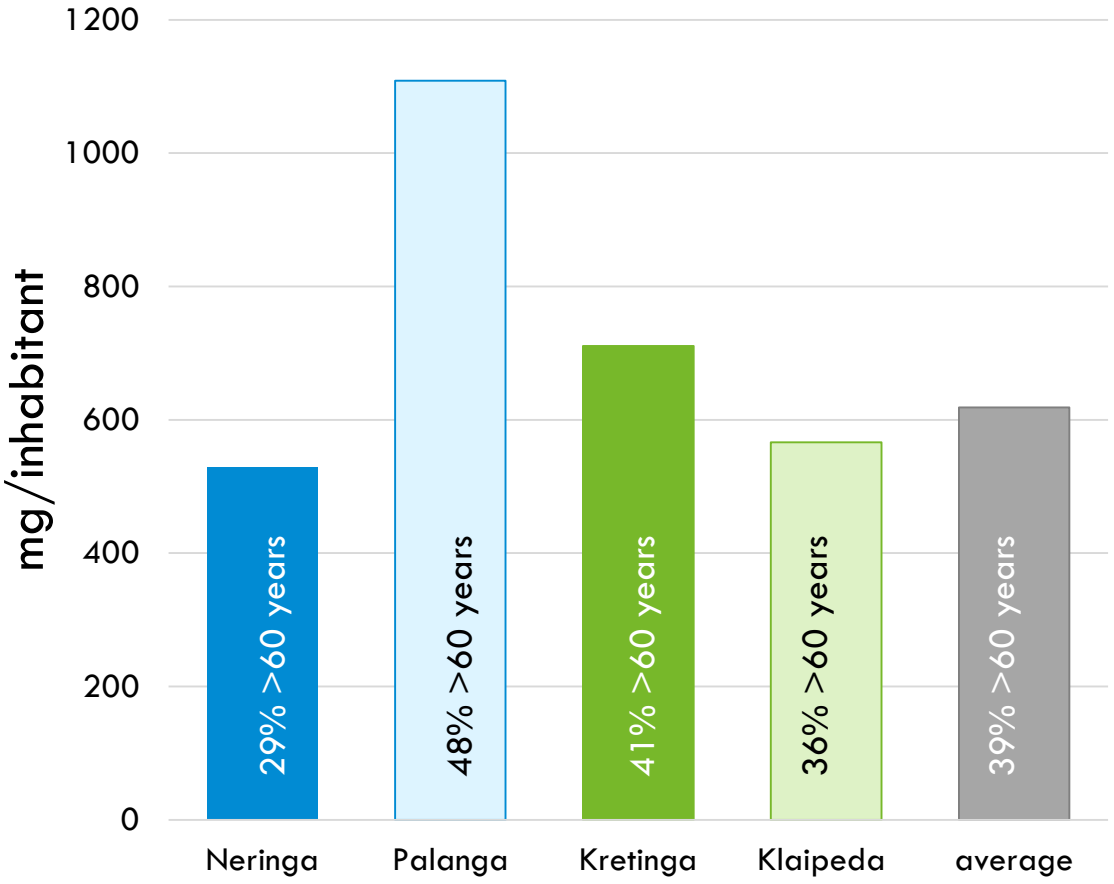


seasonal

steady



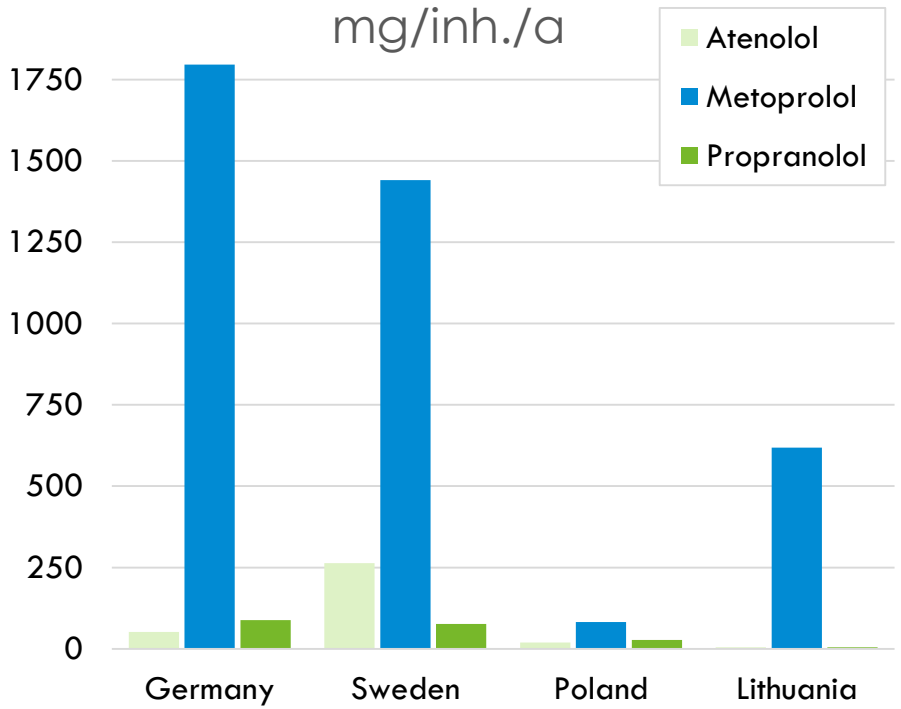
Results: Spatial Resolution in Lithuania



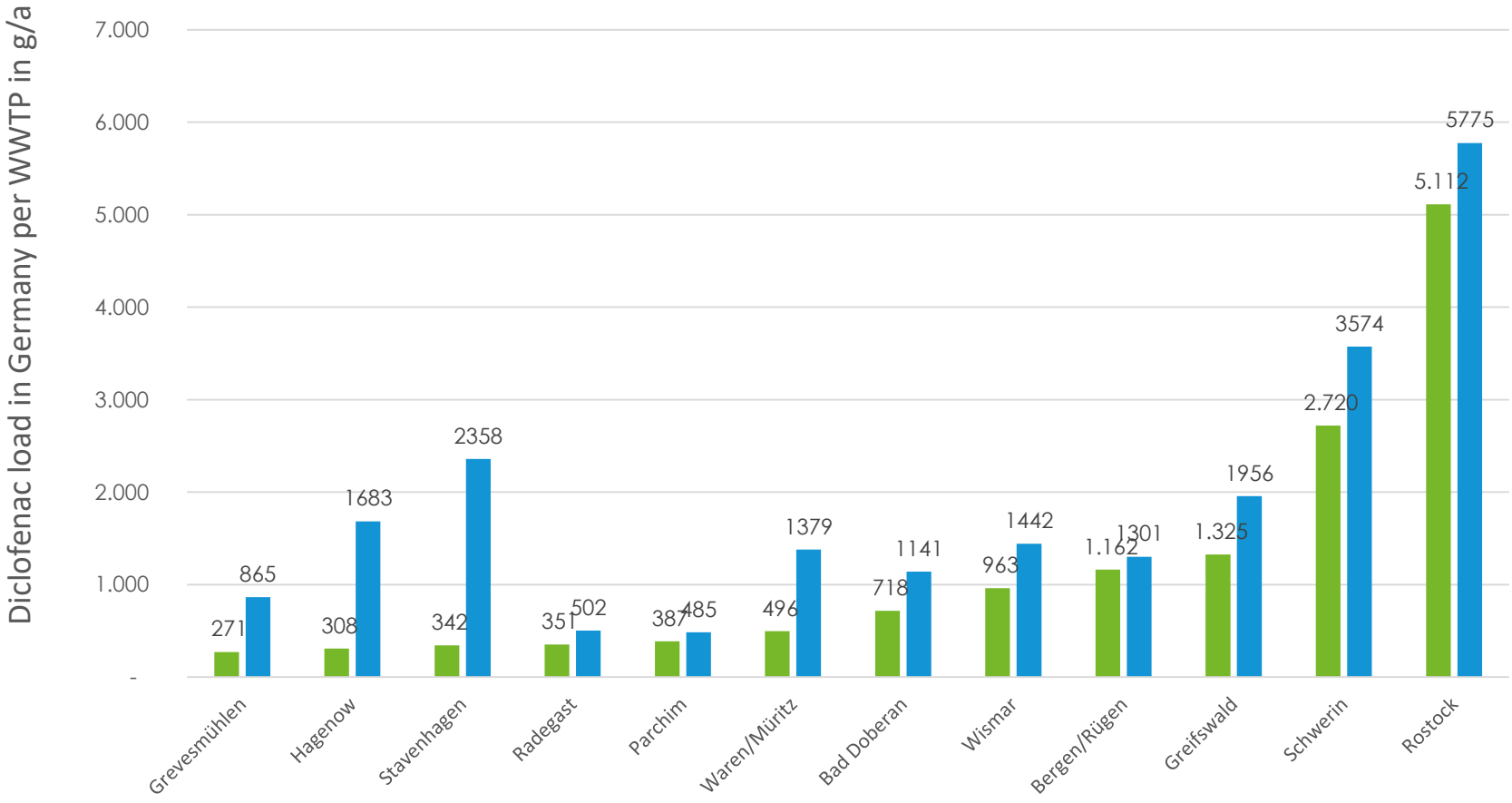
Correlation of intake and demography

Results: Comparison

Pharmaceutical	Germany [mg/inh.]	Sweden [mg/inh.]	Poland [mg/inh.]	Lithuania [mg/inh.]
Amoxicillin	840.9	414.7	2,952.9	977.3
Atenolol	51.8	262.8	19.3	4.2
Azithromycin	82.0	9.8	73.0	7.6
Bezafibrate	163.4	31.4		
Carbamazepine	892.7	526.6	715.9	204.1
Ciprofloxacin	365.1	298.6	251.0	84.5
Clarithromycin	205.8	13.4	226.7	66.4
Diclofenac	616.2	334.4	210.1	257.7
Erythromycin	350.3	50.1		0.9
Estradiol	3.3		0.8	
Ethinylestradiol	5.4			
Fluoxetine	11.4	46.0	20.0	2.3
Ibuprofen	12,610.4	10,585.6	223.6	2,001.6
Iopromide	19,551.7			
Metformin	29,621.5	15,459.0	17,602.7	9,606.2
Metoprolol	1,796.1	1,441.2	82.2	618.7
Naproxen	261.4	1,108.6	780.4	135.4
Oxazepam	1.0	69.6		1.4
Paracetamol	882.9	58,416.1		968.6
Propranolol	87.7	76.7	27.6	4.3
Risperidone	3.0	1.4	1.2	1.2
Sulfamethoxazole	260.9	238.2	149.6	47.3

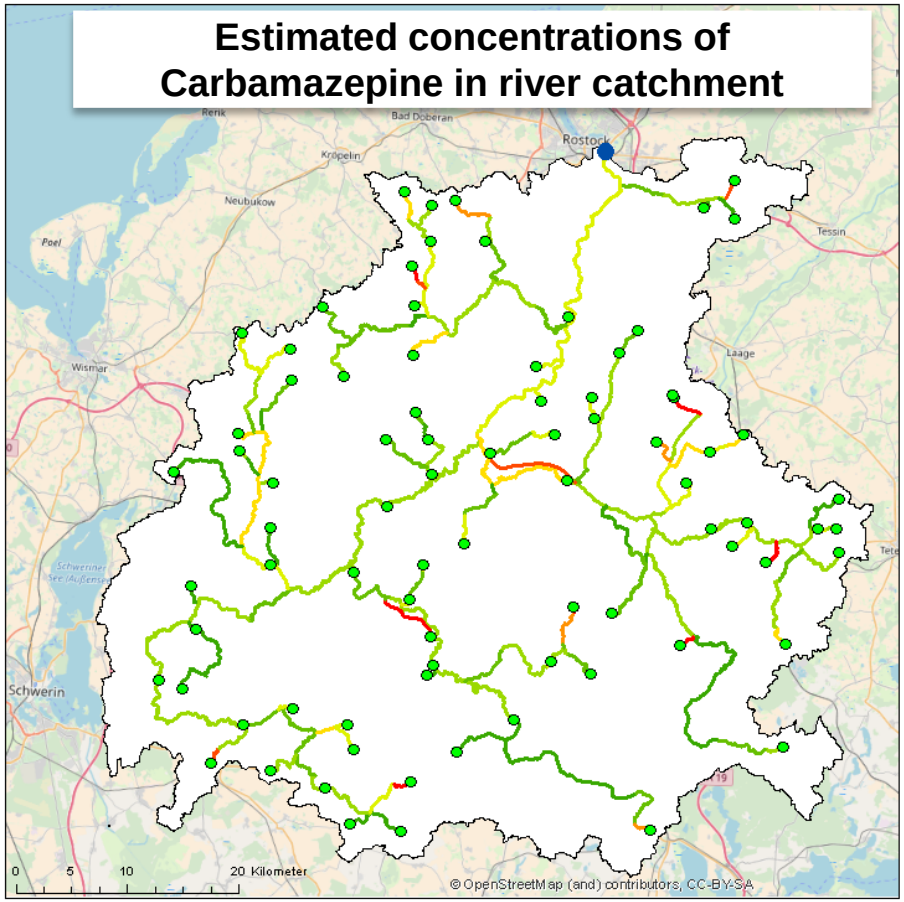


Follow-up for Model Approach



Follow-up for Model Approach

- Intake per inhabitant projection on WWTP
- Scenario: many WWTPs in catchment
- **Accumulation** of loads in rivers discharging into the Baltic Sea
- Predictable concentrations
- Applicable for all Model Areas



Source: masterthesis E.Wiktorowski 2018 (Universität Rostock)

Conclusion

1. With given data quality and availability, a proper consumption analysis can be performed.
2. Model approaches need to be adjusted to national data formats but can be made comparable (intake mg/inh./a).
3. Consumption can be predicted at WWTP level via connected inhabitants.
4. In rural areas, mitigation strategies become more challenging due to dispersed point sources.
5. By using average but regional loads, a basic model was developed with optimization potential for scenarios in rural areas.

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Thank you for your attention and now time for Q&A

WP3 Regional Consumption Patterns of Pharmaceuticals

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