WP3 – Regional Consumption Patterns of Pharmaceuticals

PP3
Jens Tränckner and Alena Kaiser
(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

<table>
<thead>
<tr>
<th>J – Antiinfectives for systemic use</th>
<th>N – Nervous system</th>
<th>C – Cardiovascular system</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>Paracetamol</td>
<td>Atenolol</td>
</tr>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>M – Muscolo-skeleton system</th>
<th>G – Genito urinary system and sex hormones</th>
<th>A – Drugs used in diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diclofenac</td>
<td>Estradiol</td>
<td>Metformin</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>Estrone</td>
<td></td>
</tr>
<tr>
<td>Naproxen</td>
<td>Ethinylestradiol</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| 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!

<table>
<thead>
<tr>
<th>Pharmaceutical</th>
<th>ATC</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diclofenac</td>
<td>D11AX18</td>
<td>Dermatologicals</td>
</tr>
<tr>
<td></td>
<td>M01AB05</td>
<td>Muscolo-skeletal system Antiinflammatory and antirheumatic, non-steroids</td>
</tr>
<tr>
<td></td>
<td>M01AB55</td>
<td>Acetic acid derivatives and related substances</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>N02AJ05</td>
<td>Nervous system Analgesics, opioids</td>
</tr>
<tr>
<td></td>
<td>N02AJ50</td>
<td>Opioids in combination with non-opioid analgesics</td>
</tr>
</tbody>
</table>
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
Inhabitants of Federal State MV in 2015

Pharmaceutical intake load per year [mg/inh] per inhabitant

Pharmaceutical intake DDD per year (only prescription)

Identification via ATC code

Federal State MV

ATC-DDD-Index (g/DDD)

IQVIA data

Pharmaceutical intake DDD per year (private and statutory prescription, hospitals, OTC)

Total pharmaceutical intake load per year in Federal State MV [kg]

loadMV
inhabitantsMV

Pharmaceutical intake load per year per inhabitant [mg/inh]

Inhabitants model area Mecklenburg in 2015

Total pharmaceutical intake load per year in model area [kg]

loadinh × inhabitantsMecklenburg

Literature/received data

Calculations
Model Approach SE-model area

**Socialstyrelsen Consumption data**

**Region Skåne**

**Identify via ATC code**

\[ \sum \text{pharmaceutical}_{ATC} \]

**Region Skåne – Internal data**

**Pharmaceutical intake DDD per year (only prescription)**

**Pharmaceutical intake DDD per year (prescription, hospitals, OTC)**

\[ \text{intake}_{\text{DDD, Skåne}} \times \text{Index}_{ATC/\text{DDD}} \]

**Inhabitants of Region Skåne in 2015**

**Inhabitants Kristianstad Municipality in 2015**

**Total pharmaceutical intake load per year in Skåne**

\[ \frac{\text{load}}{\text{inhabitants}_{\text{Skåne}}} \]

**Pharmaceutical intake load per year per inhabitant**

\[ \frac{\text{load}_{\text{inh}} \times \text{inhabitants}_{\text{Kristianstad}}}{\text{inhabitants}_{\text{Skåne}}} \]

**Total pharmaceutical intake load per year in model area**

\[ \sum \text{load}_{\text{inh}} \times \text{inhabitants}_{\text{Skåne}} \]

**calculations**

**literature/received data**
Identification of Pharmaceutical by EAN code

Model Area within Voivodship Pomerania (5 counties)

Inhabitants of model area in 2015

Pomerania Voivodship

Inhabitants of voivodship Pomerania in 2015

Content of package (pharmaceutical load)

Amount of reimbursed packages per month

Pharmaceutical intake load per month

\[ \sum m_{\text{pharma}} \]

Pharmaceutical intake load per year (2015)

\[ \frac{m_{\text{pharma}}}{\text{inh}_{POM}} \]

Pharmaceutical intake load per year per inhabitant

\[ m_{\text{inh}} \times \text{inh}_{MA} \]

Total pharmaceutical intake load per year

content of package

\[ c_{\text{pharma}} \times n_{\text{pills}} \]

\[ c_{\text{pharma}} \times V_{\text{liquid}} \]

calculation

literature/ received data
Model Approach for LT-model area

- **REGIONAL DATA (NHIF)**
  - Amount of reimbursed packages per year
  - Coastal county (e.g. Palanga)
  - Model Area 4 coastal counties

- **Identification via ATC code**
  - $c_{\text{pharma}} \times n_{\text{pills}}$
  - $c_{\text{pharma}} \times V_{\text{liquid}}$

- **Content of package (pharmaceutical load)**
  - $m_{\text{pharma}} \times N_{\text{packages}}$

- **Pharmaceutical intake load per year per county**

- **Total pharmaceutical intake load per year**

- **Inhabitants of model area**

- **Inhabitants of Lithuania**

- **Pharmaceutical intake load per year per inhabitant**

- **NATIONAL DATA (SMCA)**
  - Sales data on consumption in DDD/1000/day
  - ATC-DDD-Index (g/DDD)

- **Calculations**
  - Literature/received data

- **Total pharmaceutical intake load per year**

- **Total pharmaceutical intake load per year**

- **Total pharmaceutical intake load per year**
# Results: country-wise total intake loads

<table>
<thead>
<tr>
<th>Pharmaceutical</th>
<th>total intake in 2015</th>
<th>Intake per inhabitant</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Amoxicillin</strong>*</td>
<td>63</td>
<td>414.7</td>
</tr>
<tr>
<td><strong>Atenolol</strong></td>
<td>2</td>
<td>262.8</td>
</tr>
<tr>
<td><strong>Azithromycin</strong></td>
<td>34</td>
<td>9.8</td>
</tr>
<tr>
<td><strong>Carbamazepine</strong></td>
<td>11</td>
<td>31.4</td>
</tr>
<tr>
<td><strong>Ciprofloxacin</strong></td>
<td>9</td>
<td>528.6</td>
</tr>
<tr>
<td><strong>Clarithromycin</strong></td>
<td>32</td>
<td>298.6</td>
</tr>
<tr>
<td><strong>Diclofenac</strong></td>
<td>22</td>
<td>13.4</td>
</tr>
<tr>
<td><strong>Estradiol</strong></td>
<td>6</td>
<td>334.4</td>
</tr>
<tr>
<td><strong>Ethylnlestradiol</strong></td>
<td>8</td>
<td>50.1</td>
</tr>
<tr>
<td><strong>Fluoxetine</strong></td>
<td>10</td>
<td>0.2</td>
</tr>
<tr>
<td><strong>Ibuprofen</strong></td>
<td>4</td>
<td>46.0</td>
</tr>
<tr>
<td><strong>Iopromide</strong></td>
<td>22</td>
<td>10585.6</td>
</tr>
<tr>
<td><strong>Metformin</strong></td>
<td>22</td>
<td>15459.0</td>
</tr>
<tr>
<td><strong>Metoprolol</strong></td>
<td>3</td>
<td>1441.2</td>
</tr>
<tr>
<td><strong>Naproxen</strong></td>
<td>24</td>
<td>1108.6</td>
</tr>
<tr>
<td><strong>Oxazepam</strong></td>
<td>2</td>
<td>69.6</td>
</tr>
<tr>
<td><strong>Paracetamol</strong></td>
<td>5819.9</td>
<td>58416.1</td>
</tr>
<tr>
<td><strong>Propanolol</strong></td>
<td>2</td>
<td>76.7</td>
</tr>
<tr>
<td><strong>Risperidone</strong></td>
<td>53</td>
<td>1.4</td>
</tr>
<tr>
<td><strong>Sulfamethoxazole</strong></td>
<td>19.7</td>
<td>238.2</td>
</tr>
</tbody>
</table>
Various Distribution Sites of Pharmaceuticals in Sweden and Germany

Ibuprofen
- Sweden: 81.8% OTC, 17.7% prescribed, 0.5% hospital
- Germany: 63.4% OTC, 31.4% prescribed, 4.2% hospital

Ciprofloxacin
- Sweden: 85% OTC, 15% prescribed
- Germany: 75% OTC, 25% prescribed

December 13, 2019
Results: Temporal Resolution in Poland

Amoxicillin (antibiotic) - Seasonal

Metformin (antidiabetic) - Steady
Results: Spatial Resolution in Lithuania

Correlation of intake and demography

December 13, 2019
### Results: Comparison

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

![Graph showing comparison of pharmaceutical usage in different countries](image)

*Germany, Sweden, Poland, Lithuania*
Follow-up for Model Approach

Diclofenac load in Germany per WWTP in g/a

- Grevesmühlen
- Hagenow
- Stallenhagen
- Radelgast
- Parchim
- Waren/Müritz
- Bad Doberan
- Wismar
- Bergen/Rügen
- Greifswald
- Schwerin
- Rostock

- 271
- 308
- 342
- 351
- 385
- 496
- 718
- 963
- 1379
- 1683
- 2358
- 3574
- 5775

DICLOFENAC load in Germany per WWTP in g/a
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

Estimated concentrations of Carbamazepine in river catchment

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

WP3 Regional Consumption Patterns of Pharmaceuticals

Jens Tränckner & Alena Kaiser

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