

# Oral Antibiotics in Germany and the Netherlands in Primary Care from 2012 – 2016: A Comparison

Gabriele Gradl<sup>1</sup>, Martina Teichert<sup>2</sup>, Marita Kieble<sup>1</sup>, Johanna Werning<sup>1</sup>, Martin Schulz<sup>1</sup>

**LU** Leiden University (1) German Institute for Drug Use Evaluation (DAPI), Berlin, Germany.  
**MC** Medical Center (2) Department of Clinical Pharmacy & Toxicology, Leiden University Medical Center, Leiden, the Netherlands.

**DAPI**  
Deutsches Arzneiprüfungsinstitut e.V.

## Background and Objective

Overuse of antibiotics is of concern, but may differ between countries. This study compares the use of oral antibiotics in Germany (DE) and the Netherlands (NL) in primary/ambulatory care where the majority is used (EU/EEA: 22.4 defined daily doses per 1,000 inhabitants per day (DID) compared to 2.1 DID in the hospital sector [1]).

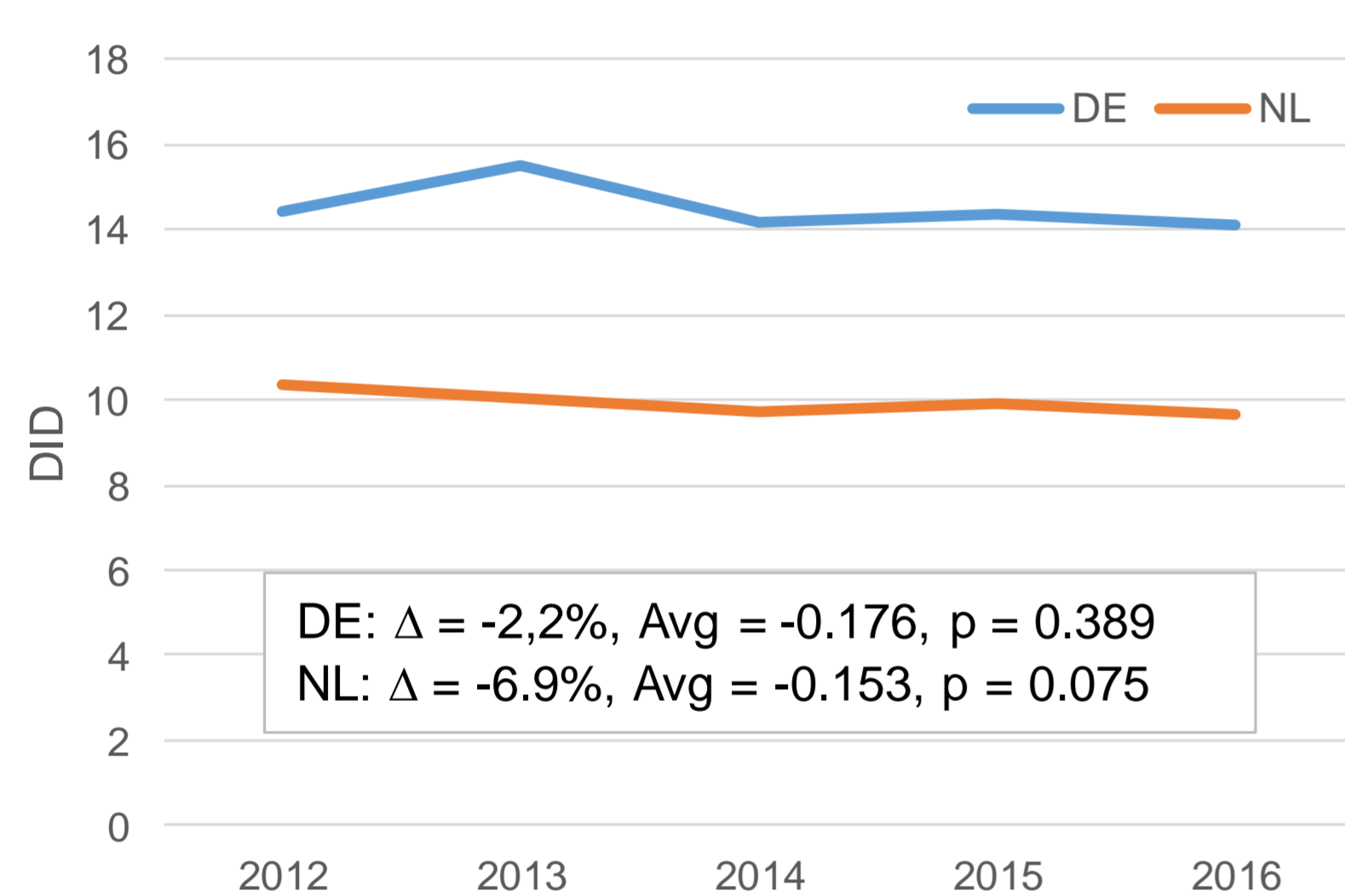
## Methods

- Longitudinal drug utilization study of oral antibiotics during the years 2012 to 2016 in DE and NL.
- DE: DAPI database containing dispensings at the expense of the Statutory Health Insurance Funds from > 80% of community pharmacies.
- NL: Data from the Dutch Foundation for Pharmaceutical Statistics, that collects dispensings from nearly 95% of community pharmacies in the Netherlands.
- Use of oral antibiotics was estimated as DID, except for comparison of age groups as packages per 1,000 inhabitants per year.
- National time trends were assessed with linear regression for overall use, stratified for the major antibiotic classes (penicillins, cephalosporins, tetracyclines, quinolones, macrolides, and lincosamides), and individual substances.

## Results

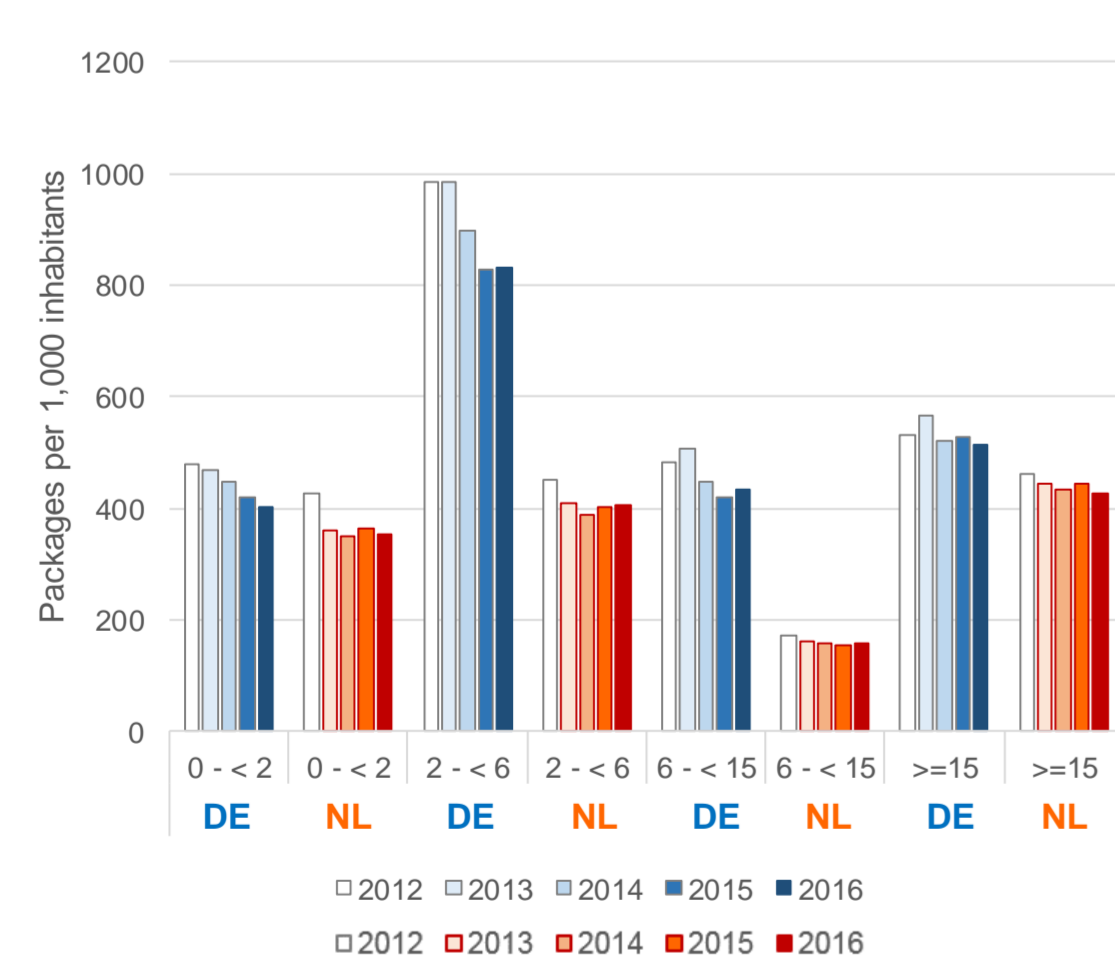
### Overall use

- In 2016, 14.1 DID of oral antibiotics were dispensed in DE compared to 9.6 DID in NL ( $\Delta = -2.2\%$  in DE and  $-6.9\%$  in NL, **Figure 1**).



**Figure 1:** Dispensing of oral antibiotics in DE and NL 2012 – 2016.  $\Delta = 2016$  vs. 2012, Avg = average annual change.

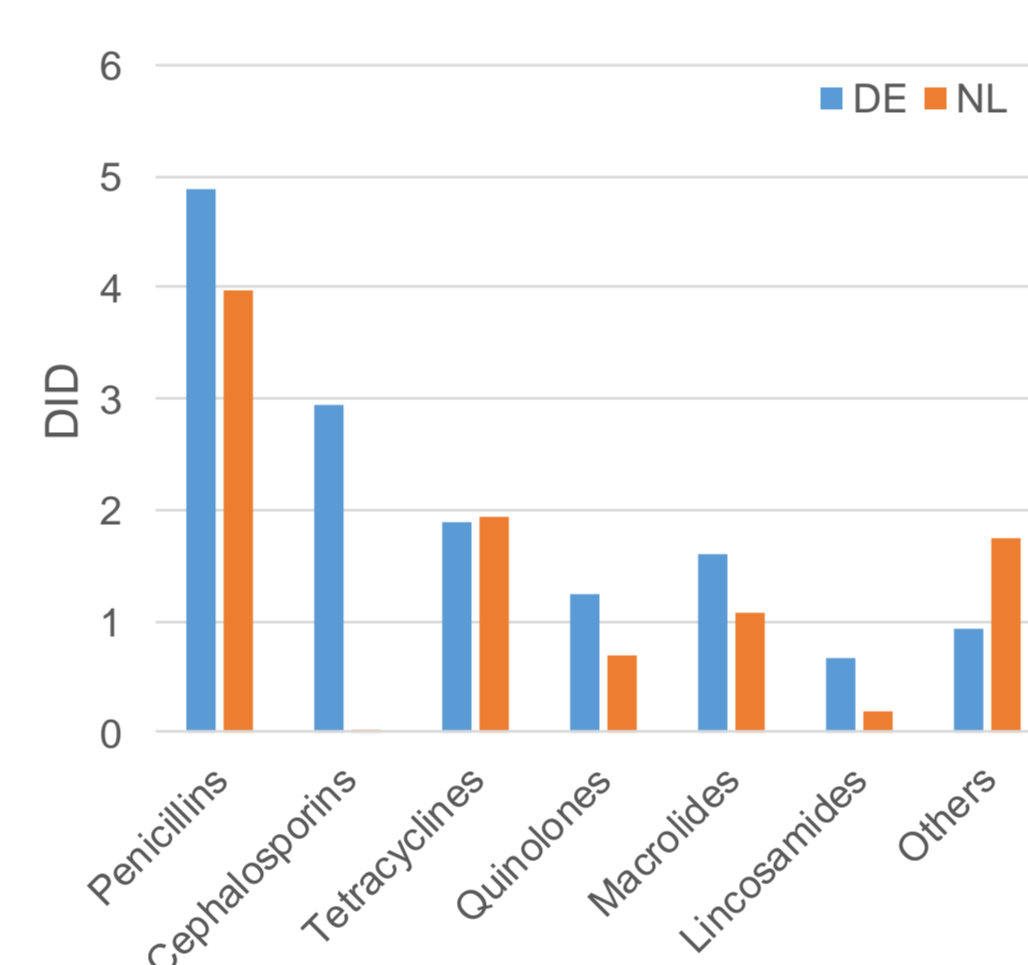
- In DE, dispensing of oral antibiotics to children was higher compared to NL, especially for the age groups 2 to 6 years and 6 to 15 years (**Figure 2**).



**Figure 2:** Age-stratified oral antibiotic dispensings 2012–2016.

### Major antibiotic classes

- Cephalosporin** use is very low in the Netherlands, but the second frequent class dispensed in Germany in 2016 (0.02 DID in NL vs. 2.95 DID in DE, **Figure 3**).



**Figure 3:** Dispensing of oral antibiotic classes in DE and NL in 2016.

- Dispensings of **lincosamides** in NL significantly increased over time (from 0.15 to 0.19 DID,  $\Delta = 27.5\%$ ,  $p=0.001$ ) but decreased in DE (from 0.75 to 0.65 DID,  $\Delta = -10.7\%$ ,  $p=0.014$ ).
- Dispensing of quinolones, tetracyclines, and other antibiotics (including sulfonamides / trimethoprim, aminoglycosides, glycopeptides, fosfomycin and nitrofurantoin derivatives) in DE and cephalosporins and tetracyclines in NL showed a statistically significant decrease.

### Individual substances

- In 2016, **amoxicillin** was the most frequently dispensed antibiotic in both countries (**Tables 1 and 2**).
- Three of the 10 most frequently dispensed oral antibiotics in both countries (ciprofloxacin, azithromycin and clarithromycin) belong to the watch group antibiotics according to the WHO [2] (**Tables 1 and 2**).

**Table 1:** 10 most frequently dispensed oral antibiotics for DE in 2016 (ranked by DID).

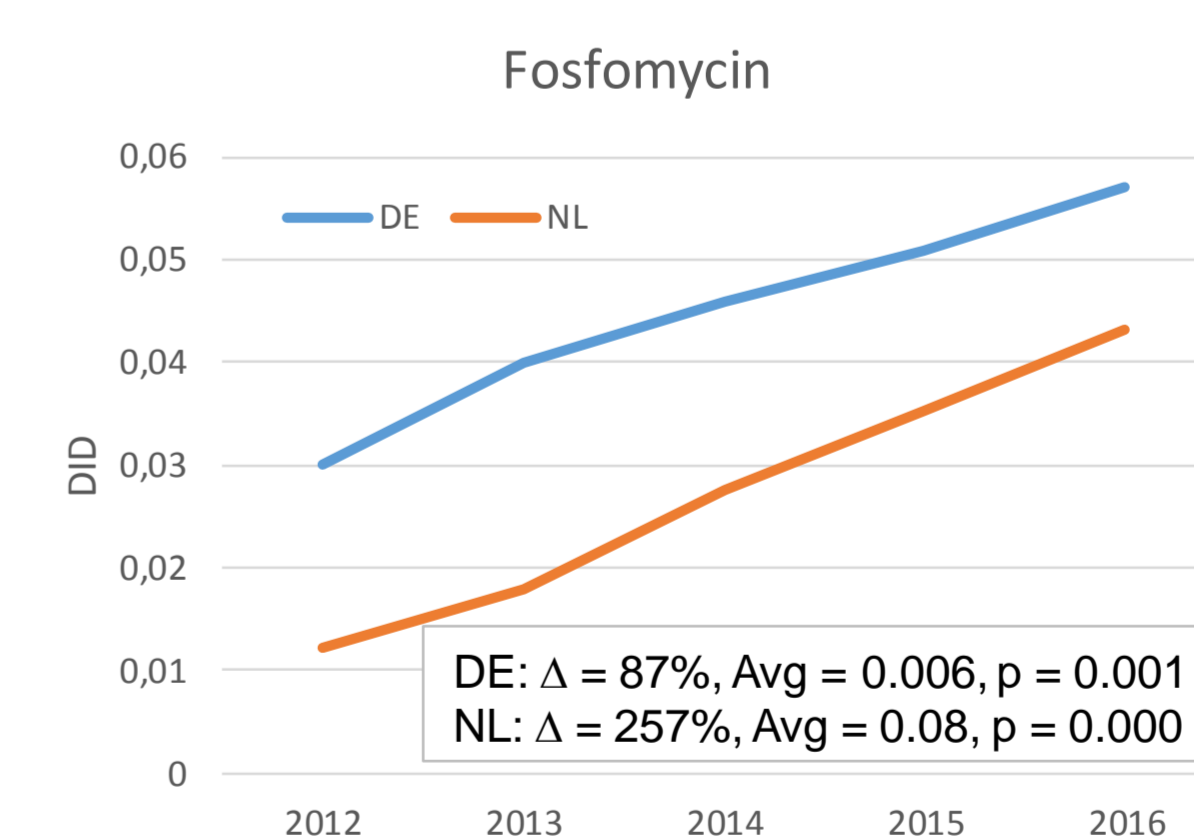
Rank	Antibiotic	NL	DE (for comparison)
1	Amoxicillin	1.92	3.45
2	Doxycycline	1.68	1.72
3	Amoxicillin and enzyme inhibitor	1.41	0.76
4	Nitrofurantoin	1.29	0.39
5	Azithromycin*	0.75	0.54
6	Ciprofloxacin*	0.56	0.73
7	Flucloxacillin	0.42	0.01
8	Clarithromycin*	0.30	0.54
9	Sulfamethoxazole and trimethoprim	0.26	0.39
10	Minocycline	0.26	0.14

**Table 2:** 10 most frequently dispensed oral antibiotics for NL in 2016 (ranked by DID).

Rank	Antibiotic	DE	NL (for comparison)
1	Amoxicillin	3.45	1.92
2	Cefuroxime	2.26	0.01
3	Doxycycline	1.72	1.68
4	Amoxicillin and enzyme inhibitor	0.76	1.41
5	Ciprofloxacin*	0.73	0.56
6	Clindamycin	0.67	0.19
7	Phenoxymethylpenicillin	0.55	0.01
8	Azithromycin*	0.54	0.75
9	Clarithromycin*	0.54	0.30
10	Nitrofurantoin	0.39	1.29

\* Watch group antibiotics (antibiotics according to WHO that have higher resistance potential and so are recommended only for a specific, limited number of indications as first or second treatment choices).

- Fosfomycin** showed the highest increase from 2012 to 2016 in both countries (**Figure 4**).



**Figure 4:** Oral fosfomycin dispensings for DE and NL 2012 - 2016.  $\Delta = 2016$  vs. 2012, Avg = average annual change.

## Discussion and Conclusions

- From 2012 to 2016, overall use of oral antibiotics in the Netherlands was much lower than in Germany. Antibiotic use in primary care in both countries decreased slightly over time.
- High level of oral cephalosporin dispensings in Germany cannot be explained by national guidelines. In the Netherlands and following the guidelines, oral cephalosporins were hardly used at all.
- Fosfomycin dispensings increased both in DE and NL. Due to its low risk of selection of multiresistant pathogens and bacteriological collateral damage it is recommended in both countries to treat uncomplicated urinary tract infections.

## References:

- [1] Summary of the latest data on antibiotic consumption in the European Union, European Centre for Disease Prevention and Control, Stockholm, 2016. <https://ecdc.europa.eu/en/publications-data/summary-latest-data-antibiotic-resistance-eu-2016>, last accessed 5 September 2017
- [2] WHO Model List of Essential Medicines. 20<sup>th</sup> List (March 2017), <http://www.who.int/medicines/publications/essentialmedicines/en/>, last accessed 6 September 2017

## Conflict of interest:

None declared.

For additional information, please contact [info@dapi.de](mailto:info@dapi.de)