Trends in veterinary antibiotic use in the Netherlands 2004-2012

Updated report based on preliminary data of the first half year of 2012

Report to be published on the MARAN website www.maran.wur.nl: 9 November 2012.
This is a publication of LEI Wageningen UR.

The MARAN website provides detailed data on the trends in antibiotic use per animal species. The information presented on the website is based on data from ongoing surveillance systems on the sales and use of antimicrobial agents in animal husbandry in the Netherlands.

LEI project team

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- the veterinarians and farmers who have provided usage data.

Summary

During the period 2009-2012 the total sales of antibiotics dropped by 51%, from 495 tonnes in 2009 to an estimated 244 tonnes in 2012 (FIDIN, 2012). This already exceeds the policy objective for 2013 set by the Dutch government, i.e., a 50% reduction in antibiotic use compared with 2009. Survey data on antibiotic use per animal species indicate a further decrease in all five livestock sectors examined in the first six months of 2012.

Trends in total sales
Based on semester of 2012 (1-1-2012 to 1-7-2012) the total sales of antibiotics in the veterinary sector in 2012 are estimated to be 51% below the level of 2009. This means a decrease in the total sales of antibiotics, licensed for therapeutic use in animals in the Netherlands, from 495 tonnes in 2009 to an estimated 244 tonnes in 2012 (FIDIN, 2012). So the policy objective for 2013 - a 50% reduction compared with 2009 - may already be reached in 2012.

Trends in use per species
In 2012, as estimated based on the first semester, all five studied livestock sectors in the Netherlands showed a further decrease in antibiotic use. The trends over the last years are:
- sow/piglet farms: strong decrease, levelled off a bit in 2012;
- fattening pig farms: continuous strong decrease;
- broiler farms: strong decrease, levelled off a bit in 2012;
- veal calf farms: continuous substantial decrease;
- dairy farms: annual variation, strong decrease in 2012.

1 Introduction

Aim

The objective of this study is to obtain detailed insight into the trends in the exposure of farm animals to antibiotics. This is done by monitoring both overall sales data at the national level and usage data per animal species. The results of the study can be used by the Ministry of Economic Affairs, Agriculture and Innovation for policy evaluation. In addition, the usage data can play a role in interpreting trends in antimicrobial resistance. Moreover, these data might be used to inform the European Commission.

Monitoring in the Netherlands

Monitoring of antibiotic use in the Netherlands is done in three ways. First, FIDIN, the federation of the Dutch veterinary pharmaceutical industry, annually reports the overall sales of antibiotics. Second, LEI Wageningen UR monitors the antibiotic use per animal species, on a stratified sample of farms. Third, the large animal production sectors recently implemented centralised registration systems, monitoring the use on all farms.

Monitoring in Europe

All EU member states are required to monitor antimicrobial resistance in food-producing animals of public health concern (Zoonosis Directive 2003/99/EC). Within this context, monitoring of antibiotic use is equally important. Therefore the European Medicines Agency (EMA) is trying to establish national systems for the collection of data on sales of veterinary antimicrobial agents in Europe, in a standardised way (EMA, 2010). The sales data from FIDIN are also used for the national reporting to EMA.

2 Materials and methods

2.1 Analysis of trends in total sales

FIDIN reports the total amount of antibiotics (active ingredient in kilograms) sold in the Netherlands, at the level of pharmacotherapeutic groups. The data about use of active substances are based on sales data of members of FIDIN and are estimated to cover about 98% of all sales in the Netherlands. Actual consumption can differ from the amounts sold, as a result of stockpiling and cross-border use. The figures give information about the total sales for all animals, not per individual animal species.

The EMA collects harmonised data, primarily based on overall sales of veterinary antimicrobial agents. To ensure that the sales data provided by the EU member states are harmonised, an ESVAC Data Collection Protocol has been developed and a call for data has been sent to most EU member states.[1] To fully implement the ESVAC protocol, FIDIN had to adjust the levels of active ingredients for several products, taking into account the salt and ester formulations and calculation factors of active ingredients expressed in international units. These corrections led to a reduction of the calculated total amount of active substance by approximately 4%. The sales figures as from 2010 were based on the ESVAC template; the figures of 1999 to 2009 were re-calculated and corrected accordingly.

To adjust for trends in the size of the animal population the sales of antibiotics for therapeutic use were also expressed as grams of active ingredient per kilogram of live animal weight (Figure 3.1). For this purpose the FIDIN sales data were related to the total live weight of the average number of animals present in the Dutch livestock farming sector (pigs, poultry, veal calves, other cattle and sheep). For this analysis the following average weights were used: veal calves 172 kg (i.e. the weighted average of white veal calf 164 kg and rosé veal calf 192 kg), other cattle 500 kg, turkeys 6 kg, other poultry 1 kg, fattening pigs 70 kg, sows 220 kg, piglets (< 20 kg) 10 kg, sheep 60 kg. This yields information about the trend in the sales of therapeutic antibiotics in grams per kilogram of live animal weight present in the Netherlands over the years, consequently taking yearly fluctuations in the size of the animal population into account.

The yearly average numbers of animals and its conversion into live weight are given in Table A.1 and Table A.2 of the Appendix. For the estimate 2012 the 2011 numbers were used.

2.2 Analysis of trends in use per species

Daily doses (ADD)

The use of different active ingredients measured in kilograms is not directly comparable due to their differences in antimicrobial potency, pharmacokinetics[2], and, consequently, the dosage prescription. To provide insight into the true exposure of animals to antibiotics, the use should be determined per animal species and expressed in the number of Animal Daily Dose (ADD) per animal year (Jensen et al., 2004; abbreviated: 'dd per ay'). The ADD is the defined average maintenance dose of a specified medicine per kg of a specified animal per day, applied for its main indication. This unit conforms to international developments in this field and developments in the human health sector. With the ADD approach the calculation and comparison of the total antibiotic use on different farms is possible, even when different

[1] EC Directive 2001/82/EC and Regulation 726/2004 form a legal basis for national authorities to request the pharmaceutical industry to provide data on sales of antimicrobial agents. Member states are not yet obliged to provide data about the use of veterinary antibiotics to the EC.

[2] Differences in dosage are determined by differences in potency, differences in bioavailability and distribution throughout the body.

active ingredients are involved. Expressing the use per animal year also enables comparisons of farms with different production and vacancy periods.

Furthermore, the ADD approach offers an opportunity to study the relationship between antibiotic use and the occurrence and trends in antimicrobial resistance. With an ADD approach also a comparison of countries could be possible, but only when based on reliable usage data per animal species. The now often reported difference in grams per kg of biomass, as calculated from national total sales figures, is reasonably suitable to adjust trends in the sales for changes in the size of the animal population within a country, but not for country comparisons. A comparison of countries based on overall averages is strongly influenced by animal demographics and therefore a very inaccurate indication of the true differences in antimicrobial exposure, per animal species. To get an appropriate certainty about the true differences between countries it is necessary to have reliable information about the use per animal species (Bondt et al., 2012).

Calculating the number of daily dosages

The use of different active ingredients becomes comparable when the amount of active ingredients in each antibiotic preparation is measured as the number of daily dosages. The number of daily dosages per animal year was determined by calculating the total number of kilograms of animal that can be treated with each active ingredient,[3] the so-called treatable weight. This was then divided by the total weight of the average present livestock on the farm, assuming that the average treatment is administered to animals with an average weight.[4] The following daily dosages box gives an example of the calculation of the number of daily dosages per animal year.

Example: Calculation of the number of daily dosage

For example, a farm with 150 fattening pigs with an average weight of 70.2 kg used 2 litres of antibiotic preparation X during the course of one year (X contains 40% = 400 mg/ml of active ingredient a) and 20 kg of antibiotic preparation Y (Y contains 25% = 250 mg/g of active ingredient b). Antibiotic preparation X: the defined daily dosage of active ingredient a is 10 mg per kg of animal weight per day. Antibiotic preparation Y: the defined daily dosage of active ingredient b is 50 mg per kg of animal weight per day.

Antibiotic X can be used to treat (2,000 * 400)/10 = 80,000 kg of animal weight. Antibiotic Y can be used to treat (20,000 * 250)/50 = 100,000 kg of animal weight. Consequently, the farm has used antibiotics for treatment of a total of 180,000 kg of animal weight. The farm has an average of 150 fattening pigs per year, with a total weight of 10,530 kg. 180,000 kg were treated in that year, equivalent to 180,000/10,530 = 17.1 daily dosages. Consequently, an average fattening pig[5] on the farm in that year was administered a prescribed dosage of antibiotics on 17.1 days. In this example the farm uses 17.1 daily dosages per animal year of antibiotic preparation X plus Y.

Animal weights

The calculations in the sample survey are based on the average weight per animal during the animals' presence on the farm. The following average weights have been used: dairy cows 600 kg, veal calves

[3] The use of antibiotics in spray containers is not included.
[4] The total weight is the average weight of the animals (in kg per animal) multiplied by the average number of animals present on the farm per year. Note that on dairy farms only the weight of the dairy cows has been taken into account.
[5] This refers to a pig on the farm throughout the year: however, there is no such pig. This is a method which can be used to provide for comparisons of farms with different vacancy rates. For example, a farm has 2 herds of animals a year, both of which comprise 200 animals that remain on the farm for 5.5 months. The farm is vacant during the first and last week of the year, and for 2 weeks between the two herds. The calculations for this farm are based on an average of 183 animals present on the farm. When a farm is vacant for six months and has a herd of 200 animals for six months, then the calculations are based on an average of 100 animals on the farm.

172 kg (i.e. the weighted average of white veal calf 164 kg and rosé veal calf 192 kg), broilers 1 kg, fattening pigs 70 kg, sows 220 kg, maiden gilts 107.5 kg, piglets (< 25 kg) 12.5 kg, breeding boars 350 kg (ASG, 2010). On dairy farms the number of daily dosages is based on the weight of the dairy cows only, because this category of animals gets almost all of the antibiotics. On sow farms the size of the 'population at risk' is based on the weight of all present animals (including piglets, gilts, breeding boars). For an illustrative calculation of the number of daily dosages for young calves on dairy farms (from birth to weaning at 56 days of age) the average weight of 56.5 kg has been used.

2.3 Survey data and statistical analysis

Survey data

This study uses survey data from farms in the Farm Accountancy Data Network (FADN) and additional veal calf farmers. The FADN contains a stratified sample of around 1,500 agricultural and horticultural farms in the Netherlands (Vrolijk et al., 2009). Records are made of the economic data and technical key figures of these farms. Every year a number of farms are replaced by other farms to ensure that the database of the Data Network remains representative of Dutch livestock farming. On these farms all animal-medicine data and veterinary services are recorded. This provides information about the true exposure of farm animals to antibiotics, and gives insight into the underlying factors that could explain changes in antibiotic use. In cooperation with the veal calf sector the use in veal calves is monitored in an additional random sample. On the veal calf farms detailed data were collected on the number of animals present and the amount of antibiotics used.

To ensure that the farms in the sample are representative of the whole population and to make the sampling as efficient as possible, a disproportional stratified random sampling strategy is used (Vrolijk et al., 2009). A stratified sample implies that the population is divided into a number of homogeneous groups. Subsequently, farms are selected from each of the groups. For strata with larger variation in the use of antibiotics, relatively more sample farms are selected. In the FADN sample the strata are based on both farm size and animal category. The additional sample of veal calf farms is additionally stratified for 'large integration' versus 'small integration or non-contracted farms'.

Data of 187 pig, broiler and dairy cattle farms in the FADN were used to estimate the antibiotic use in 2012, based on the first semester. As from 2007, data from veal calf farms were collected in an additional sample. See Table 2.1 for details. More detailed data are available on the LEI website (www.wageningenUR.nl/en/lei) and the MARAN website (www.maran.wur.nl).

Table 2.1	Number of sample farms taking part each year and the associated number of animals						
	Type of holding	**2007**	**2008**	**2009**	**2010**	**2011**	**2012 a)**
Number of animals	Sows/piglets	17,949	18,767	20,806	24,593	22,945	20,032
	Fattening pigs	119,922	156,098	159,104	153,887	145,418	131,129
	Broilers	2,197,716	2,508,103	2,530,313	2,244,706	2,245,689	1,768,678
	Veal calves	124,115	134,437	134,446	124,634	119,746	82,194
	Dairy cows	2,850	7,274	7,382	7,020	6,115	5,598
Number of farms	Sows/piglets	39	45	48	48	49	42
	Fattening pigs	49	77	72	64	61	55
	Broilers	29	29	28	25	26	22
	Veal calves	185	199	193	173	162	113
	Dairy cows	34	82	83	77	77	68
	Total	336	432	424	387	375	300

a) Number of sample farms in first semester of 2012.

Statistical analysis

Data from the FADN farms and the additional sample for veal calves are used to estimate the use in the whole population to obtain insight into the amount of and trends in antibiotic use on the national level. Antibiotic use per species on the national level is expressed as average number of daily dosages per average animal present on an average farm. Since the stratification is disproportional, the results have to be weighted to be representative. For each stratum the average daily dosages per animal year is determined. Then the weighted average for an animal category is calculated, based on the number of farms in the population in each stratum.

The aggregated usage data are considered to be representative for the total exposure of Dutch food-producing animals to antibiotics. The 95% confidence intervals (CI) indicate that with 95% certainty, the average antibiotic use per animal on a national level, expressed by the number of daily dosages per animal year, will lie within the upper and lower limits given. The confidence interval also indicates the variation in antibiotic use amongst farms.

In this report the usage data of all sample farms are used for statistical analysis on not only antibiotic use in each year, but also on the changes in antibiotic use over a period of two or more years. Comparing average uses of antibiotics between two years can be done in two ways: one using only farms that are in the sample for both years,[6] the other using all farms in the sample in both years. The first method usually gives better results if the majority of the farms are in the sample for both periods. This usually is the case in two consecutive years. However, if the years of comparison are further apart, the number of sample farms available in both years will be more limited. In that case, testing for significant differences can better be done by using all farms in the sample to increase the statistical power of the comparison.[7]

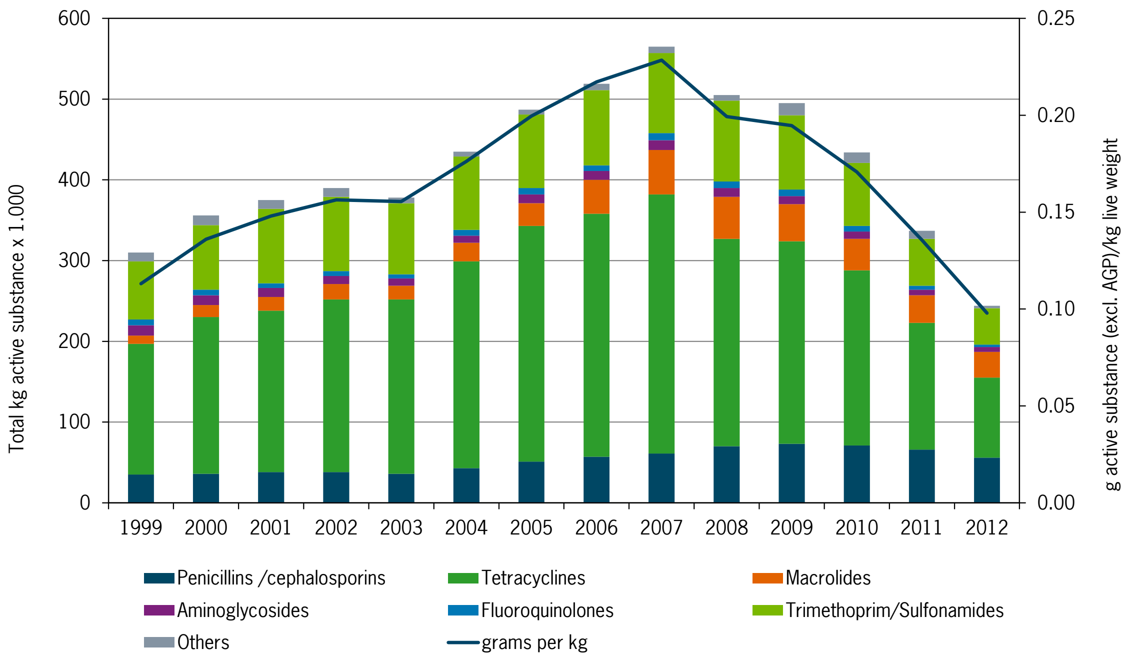
[6] See Appendix 3 in Vrolijk et al. (2008) for more details about the statistics.
[7] If the difference between the two means is larger than twice the square root of the sum of both squares of the standard errors, then there is a significant difference.

3 Trends in total sales

The total sales of antibiotics, licensed for therapeutic use in animals in the Netherlands, decreased from 495 tonnes in 2009 to an estimated 244 tonnes in 2012, which is a decrease of 51% (FIDIN, 2012). This means that the policy objective for the year 2013 - a 50% reduction compared with 2009 - will probably already be reached in 2012. Almost all classes of antibiotics showed a decrease.

Figure 3.1 shows the trend in the total sales (in bars). The trend is also expressed in grams of active substance per kg of live weight present (line), to adjust for possible fluctuations in the size of the animal population.

Figure 3.1 **Therapeutic antibiotic sales, 1999-2012 a)**



a) Sales for 2012 are estimates, based on preliminary data of the first half year.
Source: FIDIN (2012).

Discussion
The total sales volume amounted to an estimated 244 tonnes in 2012, which is substantially below the level of the year 1999. Moreover, at that time an additional 250 tonnes of antimicrobial growth promoters were used (see Table 3.1).

Tetracyclines
The sales data indicate a total decrease of 61% for tetracyclines in the period 2009-2012. The underlying detailed data show a stronger decrease of oxytetracyclines (67%) than of doxycyclines (49%).

Fluoroquinolones
In the first half year of 2012 the quinolones represented 1.3% of the total veterinary antibiotic sales in the Netherlands; the 'newer' fluoroquinolones represented 0.41% of the total sales (danofloxacin, difloxacin,

enrofloxacin and marbofloxacin). In the period 2009-2012 the sales of quinolones decreased by 59%; the newer fluoroquinolones showed a decrease of 23%.

Cephalosporins
In the first half year of 2012 the cephalosporins represented 0.10% of the total sales. In the period 2009-2012 the estimated sales of third- and fourth-generation cephalosporins (cefoperazon, cefovecin, cefquinome, ceftiofur, cefuroxim) showed an enormous decrease of 92%, to 0.03% of the total sales.

Table 3.1 **Antibiotic sales in tonnes, 1999-2012 a)**

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Penicillins/cephalosporins	35	36	38	38	36	43	51	57	61	70	73	71	66	56
Tetracyclines	162	194	200	214	216	256	292	301	321	257	251	217	157	99
Macrolides	10	15	17	19	17	23	28	42	55	52	46	39	34	32
Aminoglycosides	13	12	11	10	9	9	11	11	12	11	10	9	7	6
Fluoroquinolones	7	7	6	6	5	7	8	7	9	8	8	7	5	3
Trimethoprim/Sulfonamides	72	80	92	92	88	91	91	93	99	100	92	78	58	45
Others	11	12	11	11	7	6	6	8	8	7	15	13	10	3
Total therapeutic sales	310	356	376	390	378	434	487	519	565	506	495	433	338	244
Gram therapeutic per kg live weight	0.11	0.14	0.15	0.16	0.15	0.18	0.20	0.22	0.23	0.20	0.19	0.17	0.13	0.10
Antimicrobial growth promoters (AGP)	250	205	180	140	120	80	40	0	0	0	0	0	0	0
Total sales including AGP	560	561	556	530	498	514	527	519	565	506	495	433	338	244

Sales for 2012 are estimates, based on preliminary data of the first half year.
Source: FIDIN (2012).

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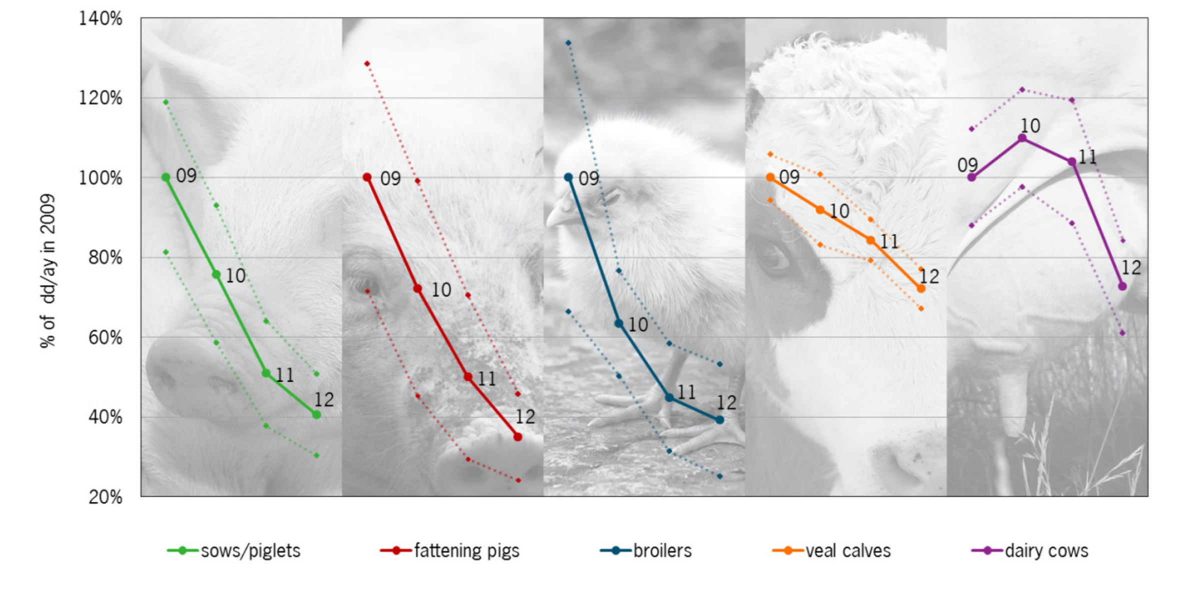
4 Trends in use per species

As shown in Figure 4.1, sample surveys reveal the following tendencies for the years 2009 to the first half year of 2012, indicating a further decrease in antibiotic use in all five studied livestock sectors in the Netherlands in 2012, when extrapolated to annual usage. The sample surveys indicate a decrease in all livestock sectors in the Netherlands in 2012. The usage data in Figure 4.1 are indexed, using 2009 as baseline year. The continuous line represents the estimated average use. The 95% confidence intervals are indicated by the dotted lines. In the paragraphs per livestock sector the results are presented from 2004 to 2012.

Figure 4.1 **Trends in antibiotic use per species, 2009-2012 a)**



a) Results for 2012 are estimates, based on preliminary data of the first half year.

Figure 4.1 shows the tendencies in antibiotic use per animal species from 2009 to 2012, indicating a further decrease in all studied livestock sectors in the Netherlands in 2012. The trends over the last years are:

- sow/piglet farms: strong decrease, levelled off a bit in 2012;
- fattening pig farms: continuous strong decrease;
- broiler farms: strong decrease, levelled off a bit in 2012;
- veal calf farms: continuous substantial decrease;
- dairy farms: annual variation, strong decrease in 2012.

For all livestock sectors the decrease in the period 2009-2012 was statistically significant.

Note that the exposure in 2012 is an estimate based on preliminary data of the first half year. Final figures about the antibiotic usage in the whole year 2012 may differ from this estimate, because of the following factors:

- analysis of more sample farms: the estimate is based on approximately 80% of the sample farms;
- structural seasonal effects: there might be seasonal differences in usage due to different weather conditions in winter, spring and early summer compared with autumn and early winter;
- incidents: antibiotic usage will be lower in case of no outbreaks of diseases or extreme beneficial weather conditions, and vice versa;
- normal stocks of veterinary medicines: the same stock has an higher impact on a half-year estimate compared with a year estimate.

Except for the first comment, the comments above also hold for the total sales data.

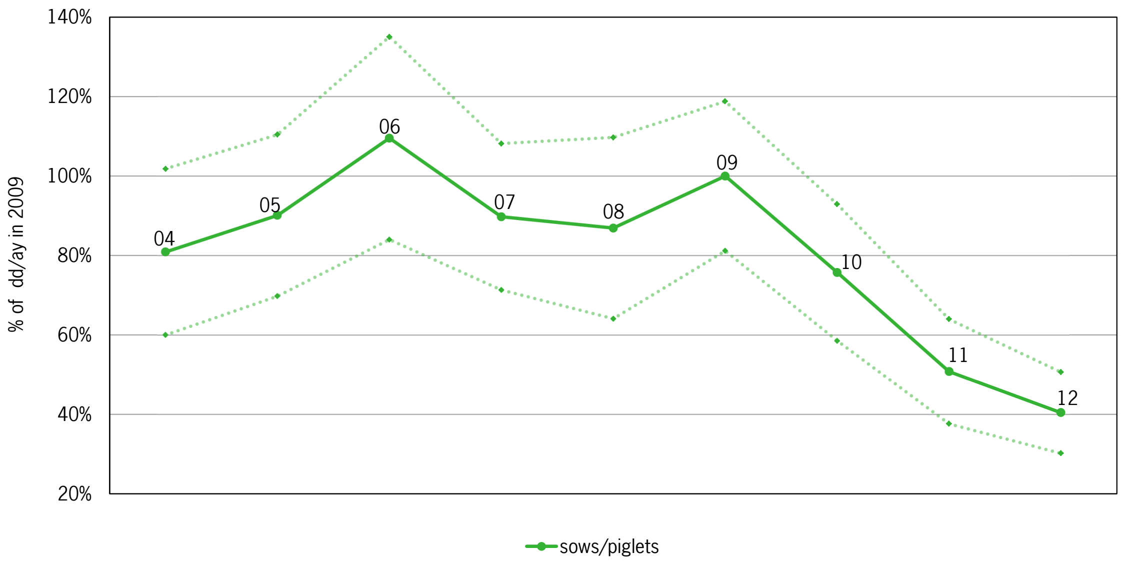
In the following paragraphs the use of the different types of antibiotics per livestock species is addressed in detail.

4.1 Pigs

Sows and piglets

Figure 4.2 shows the trend in antibiotic use from 2004 to 2012: annual variation, with a strong decrease as from 2009, which seems to level off a bit in 2012.

Figure 4.2 **Trend in antibiotic use in sows/piglets, 2004-2012 a)**

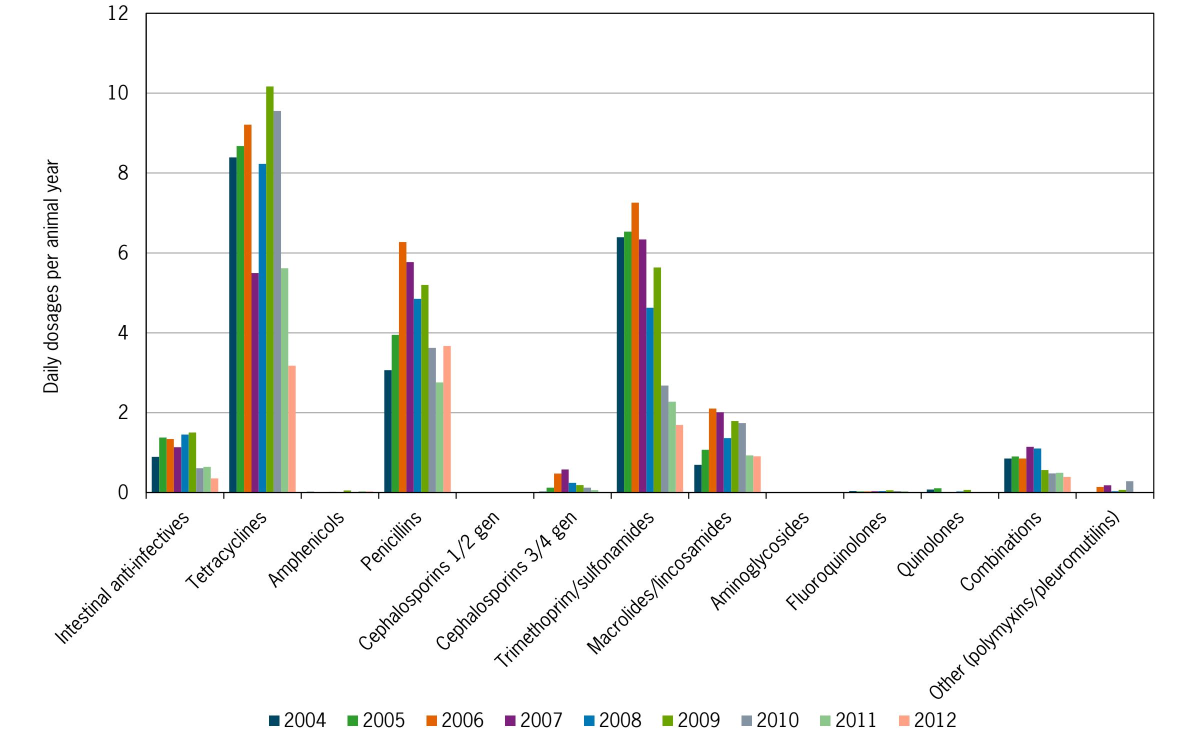


a) Results for 2012 are estimates, based on preliminary data of the first half year.

Based on the first semester, the average use in sows/piglets is estimated to be 10 daily dosages per year in 2012 (95% Confidence Interval: 8-13 dd/ay). In 2009 the use was 25 daily dosages per year (95% CI: 21-30 dd/ay). The large confidence intervals are mainly caused by the large variation in use that exists between different farms. Seventy-five per cent of the antibiotics were orally administered, probably predominantly in piglets.

Figure 4.3 provides insight into the trends in the relative use of the various groups of antibiotics.

Figure 4.3 **Antibiotic use in sows/piglets in dd per sow per year, 2004-2012 a)**

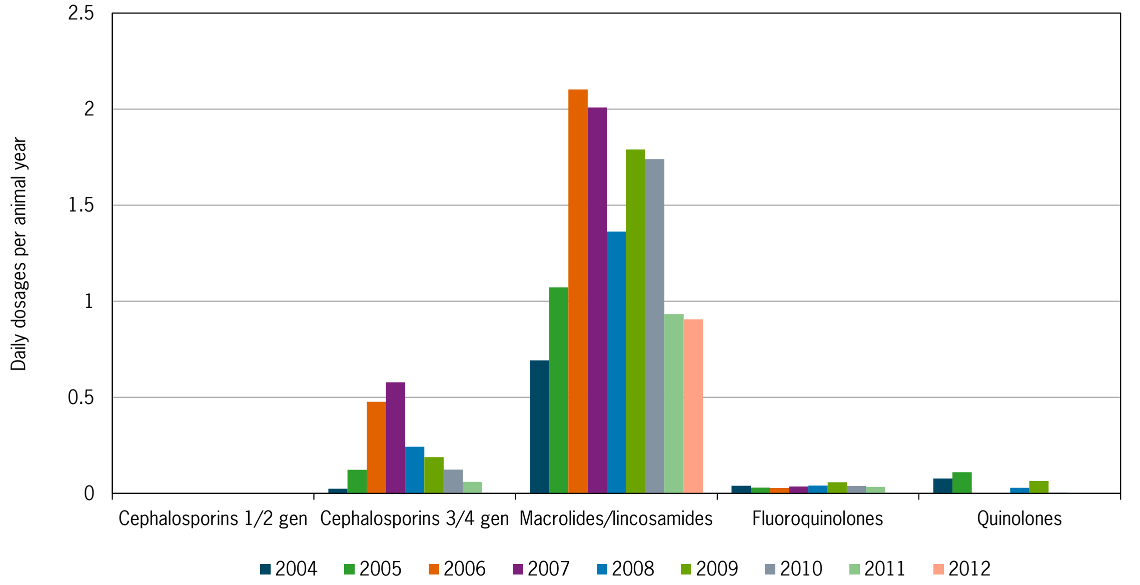


a) Results for 2012 are estimates, based on preliminary data of the first half year.

In 2012 31% of the total antibiotic use in sows/piglets consisted of tetracyclines, 36% of penicillins and another 17% of trimethoprim/sulfonamides.

Figure 4.4 shows the trends in the use of the antimicrobial classes defined as the most critically important in human medicine by the World Health Organization i.e. third- and fourth-generation cephalosporins, fluoroquinolones and macrolides. An important finding is that since 2009 the use of macrolides decreased substantially, and that in 2012 both the use of third- and fourth-generation cephalosporins and the use of fluoroquinolones in sows/piglets has dropped to zero.

Figure 4.4	Antibiotic use in sows/piglets in dd per sow per year, 2004-2012 a)



a) Results for 2012 are estimates, based on preliminary data of the first half year.

Discussion

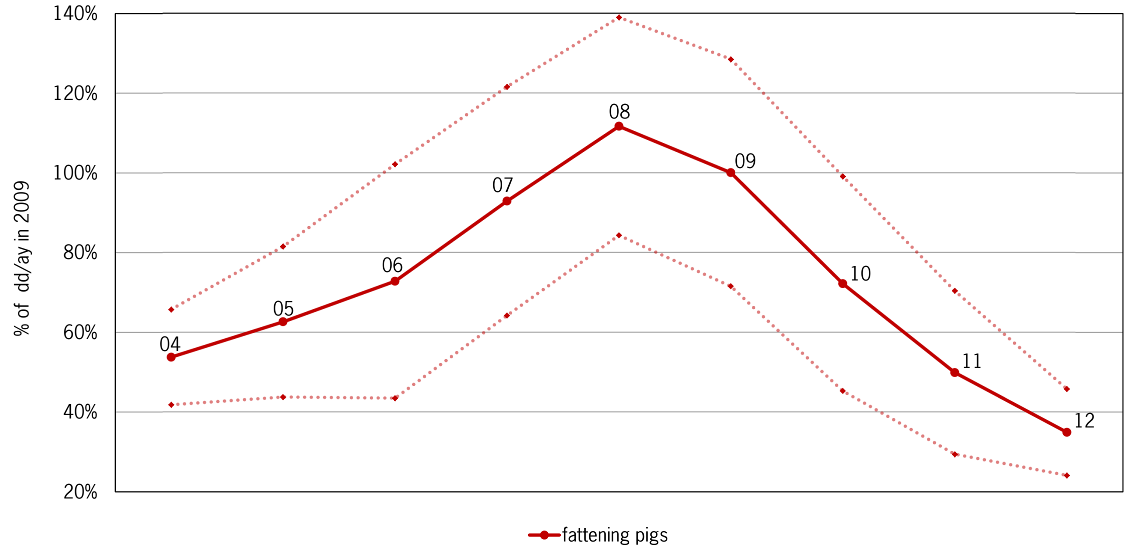
Within the sample, about 57% of the farms had an antibiotic use within the target level ('streefniveau') for 2012 of the Animal Drug Authority (SDa, 2012), 29% within the signalling level ('signaleringsniveau'), and 14% within the action level ('actieniveau').

In 2012, the use in sows/piglets was 10 daily dosages per animal year. However, in practice most antibiotics are likely used for the treatment of the piglets, and only incidentally for the sows. If it is assumed that 100% of the antibiotics are administered to the piglets, which have an average weight of 12.5 kg, this would mean that an average piglet is treated with antibiotics during 10 days in the period from birth to the age of 74 days (when the piglet weighs 25 kg and is delivered to the fattening farm).

Fattening pigs

Figure 4.5 shows the trend in antibiotic use from 2004 to 2012: increase until 2008, strong decrease from 2008 to 2012.

Figure 4.5	Trend in antibiotic use in fattening pigs, 2004-2012 a)

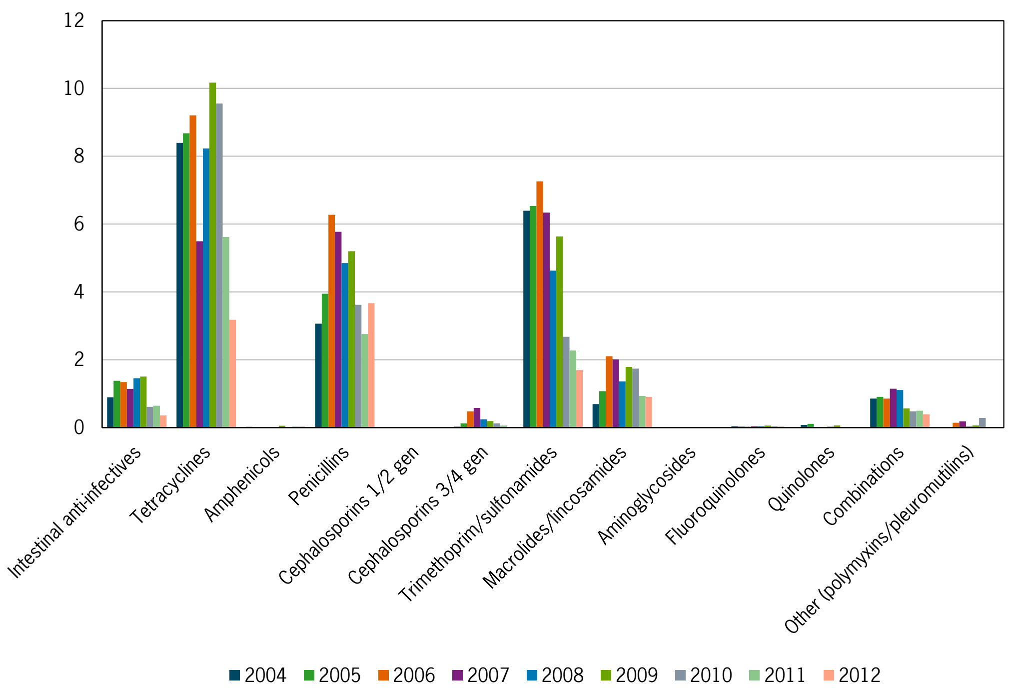


a) Results for 2012 are estimates, based on preliminary data of the first half year.

Based on the first semester, the average use in fattening pigs is estimated to be less than 6 daily dosages per year in 2012, of which 90% are orally administered (95% Confidence Interval: 4-7 dd/ay). In 2009 the average use was 16 daily dosages per year (CI: 11-20 dd/ay).

Figure 4.6 provides insight into the trends in the relative use of the various groups of antibiotics.

Figure 4.6	Antibiotic use in fattening pigs in dd per animal year, 2004-2012 a)

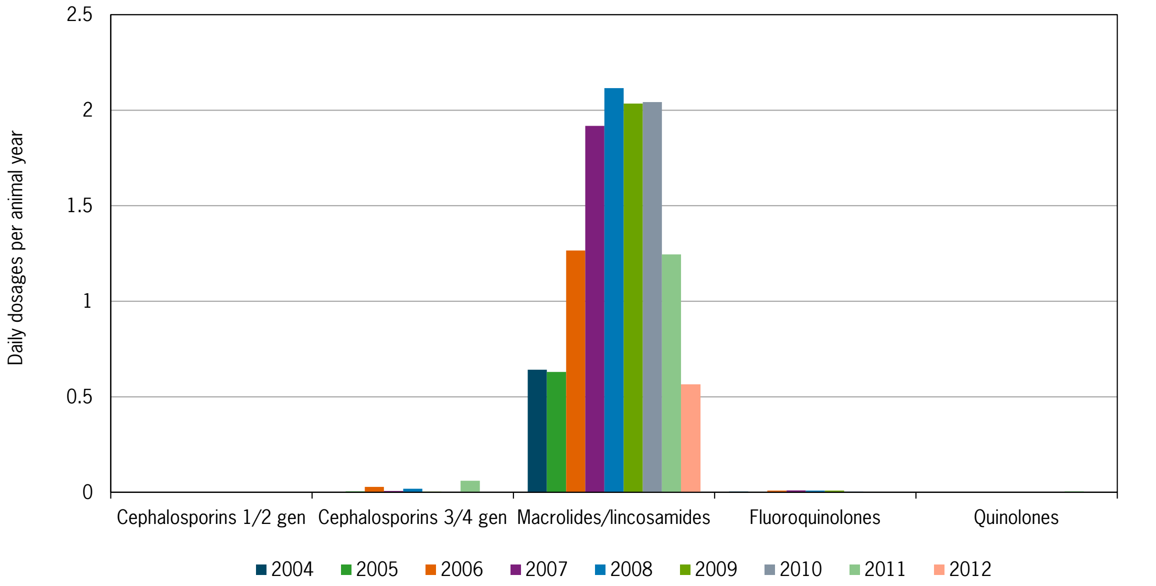


a) Results for 2012 are estimates, based on preliminary data of the first half year.

In 2012, 74% of the total antibiotic use in fattening pigs originated from the administration of tetracyclines and 10% from macrolides/lincosamides.

Figure 4.7 shows the trends in the use of the antimicrobial classes defined as the most critically important in human medicine by the World Health Organization, i.e. third- and fourth-generation cephalosporins, fluoroquinolones and macrolides. An important finding is that since 2009 the use of macrolides dropped substantially, and that in 2012 both third- and fourth-generation cephalosporins and fluoroquinolones were no longer applied.

Figure 4.7 **Antibiotic use in fattening pigs in dd per animal year, 2004-2012 a)**



a) Results for 2012 are estimates, based on preliminary data of the first half year.

Discussion

Within the sample about 69% of the farms had an antibiotic use within the target level ('streefniveau') for 2012 of the Animal Drug Authority (SDa, 2012), 11% within the signalling level ('signaleringsniveau'), and 20% fall into the action level ('actieniveau').

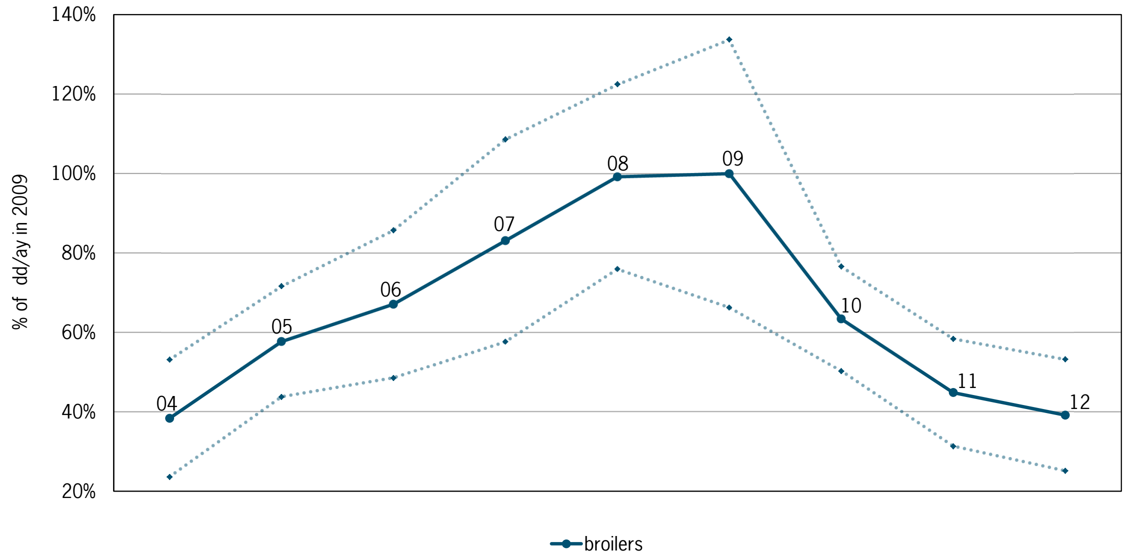
In 2012, the use in fattening pigs was approximately 6 daily dosages per animal year. Assuming a production period of 117 days, 2 daily dosages (= 6 x (117/365) are administered to each fattening pig during its production period from 25 kg to slaughter weight. This fattening pig has also received antibiotics at the breeding farm (during a maximum of 10 days), which brings the total exposure to antibiotics per fattening pig to approximately 12 days during its whole life from birth to slaughter at the age of 191 days.

If it is assumed that the average treatment weight of fattening pigs will be 30% lower than their average live weight - since younger animals are more likely to receive antibiotics than older animals - the estimation of the true exposure during the total lifetime increases from 12 days to a total of 13 days. Compared with 2009 this is a decrease of the total exposure of approximately 60%.

4.2 Broilers

Figure 4.8 shows the trend in antibiotic use from 2004 to 2012: an increase until 2008, and a strong decrease from 2009 to 2012, which seems to level off a bit in 2012.

Figure 4.8 **Trend in antibiotic use in broilers, 2004-2012 a)**

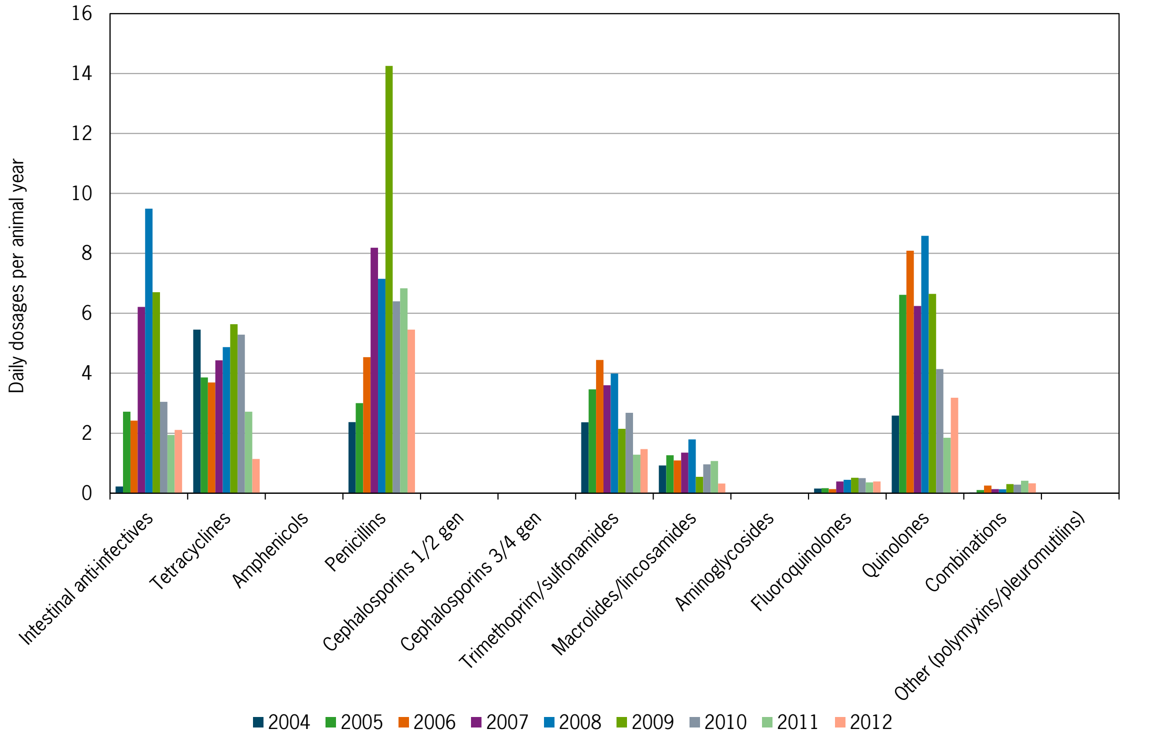


a) Results for 2012 are estimates, based on preliminary data of the first half year.

Based on the first semester, the average use in broilers is estimated to be 14 daily dosages per year in 2012, administered orally, mainly through the drinking water (95% Confidence Interval: 9-20 dd/ay). In 2009 the use was 37 daily dosages per year (CI: 24-49 dd/ay).

Figure 4.9 provides insight into the trends in the relative use of the various groups of antibiotics.

Figure 4.9 **Antibiotic use in broilers in dd per animal year, 2004-2012 a)**

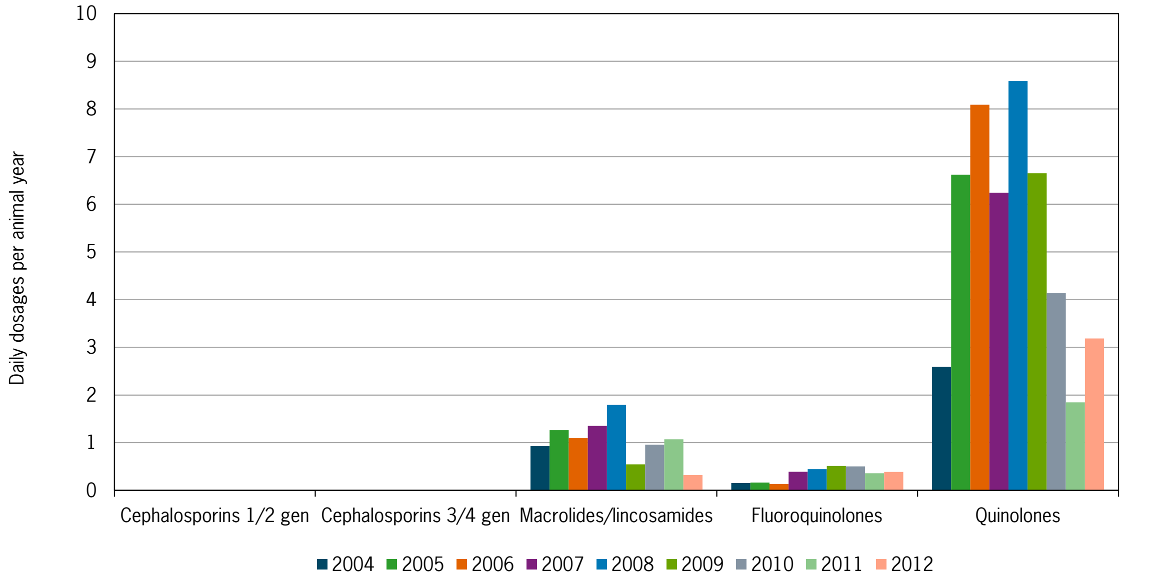


a) Results for 2012 are estimates, based on preliminary data of the first half year.

In 2012, the administration of penicillines accounted for 38% of the total antibiotic use on broiler farms, quinolones for 22%, intestinal anti-infectives for 15 % and tetracyclines for 8%. The use of intestinal anti-infectives (e.g. orally administered neomycin, colistin) decreased from 7 dd/ay in 2009 to 2 dd/ay in 2012.

Figure 4.10 shows the trends in the use of the antimicrobial classes defined as the most critically important in human medicine by the World Health Organization i.e. third- and fourth-generation cephalosporins, fluoroquinolones and macrolides. The use of macrolides and fluoroquinolones varies, and is at a relatively low level in 2012. In this year, 2.7% of the total use consisted of fluoroquinolones and 2.2% of macrolides/lincosamides. Cephalosporins were not applied.

Figure 4.10 **Antibiotic use in broilers in dd per animal year, 2004-2012 a)**



a) Results for 2012 are estimates, based on preliminary data of the first half year.

Discussion

Within the sample about 64% of the farms had an antibiotic use within the target level ('streefniveau') for 2012 of the Animal Drug Authority (SDa, 2012), 23% within the signalling level ('signaleringsniveau'), and 13% within the action level ('actieniveau').

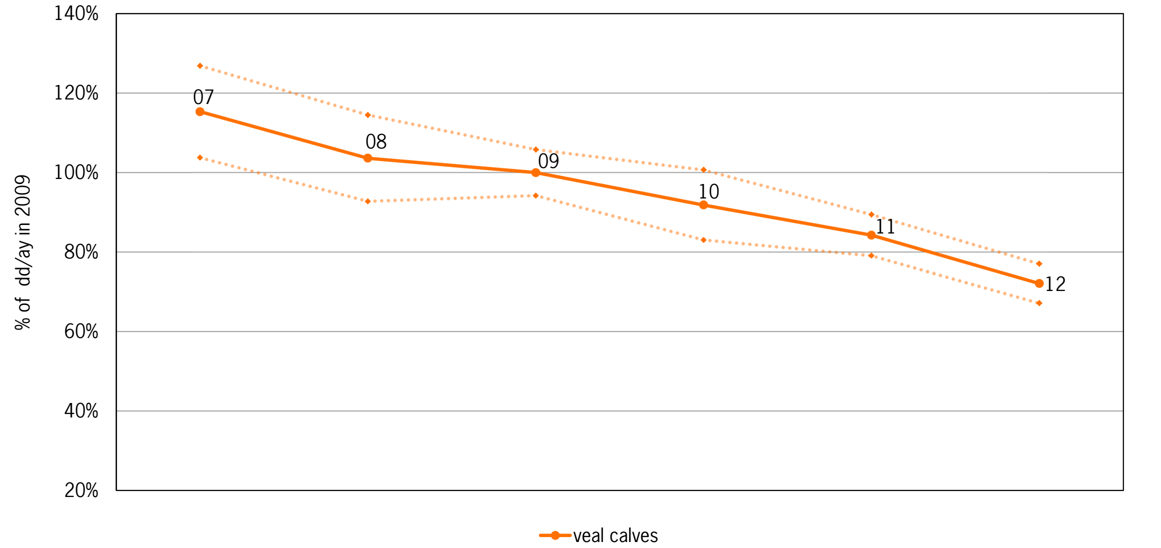
In 2012, the use was 14 daily dosages per animal year. This means that an individual broiler is treated with antibiotics during 1.6 days (= 14 x 42/365) in the 42 days from day one to slaughter.

Data on the time of prescription reveal that the average weight at which broilers receive treatment equals the average live weight of 1.0 kg. Therefore the calculated exposure of approximately 1.6 days per broiler can be considered as a reasonably adequate estimation of the true exposure (i.e. 1 to 2 treatment days per broiler, considering the 95% confidence interval).

4.3 Veal calves

Figure 4.11 shows the trend in antibiotic use in veal calves: a substantial decrease from 2007 to 2012.

Figure 4.11 **Trends in antibiotic use in veal calves, 2007-2012 a)**

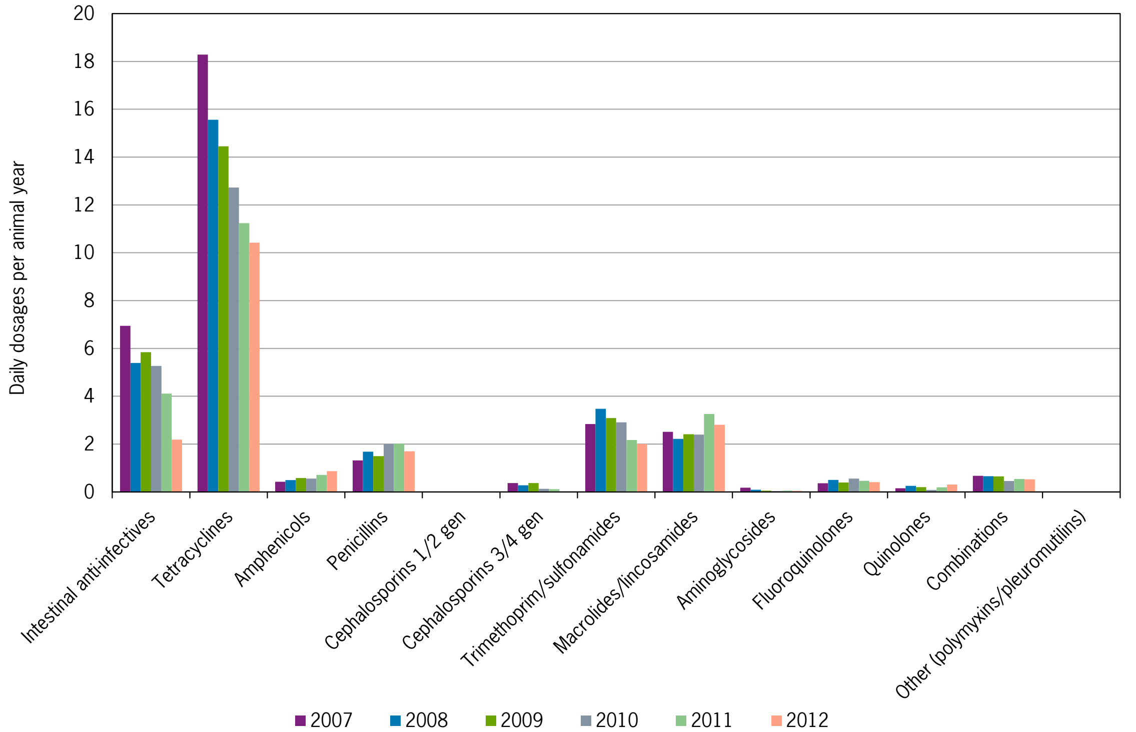


a) Results for 2012 are estimates, based on preliminary data of the first half year.

Based on the first semester, the average use in veal calves is estimated to be 21 daily dosages per animal year in 2012, of which 88% was orally administered (95% Confidence Interval: 20-23 dd/ay). In 2009 the average use was 30 daily dosages per animal year (CI: 28-31 dd/ay). The reduction in the period 2009-2012 is almost 30%. The total reduction in 2012 is 37%, compared with the start of the monitoring in veal calves in 2007. In 2007 the average use was 34 daily dosages per animal year.

Figure 4.12 provides insight into the trends in the relative use of the various groups of antibiotics.

Figure 4.12	Antibiotic use in veal calves in dd per animal year, 2007-2012 a)

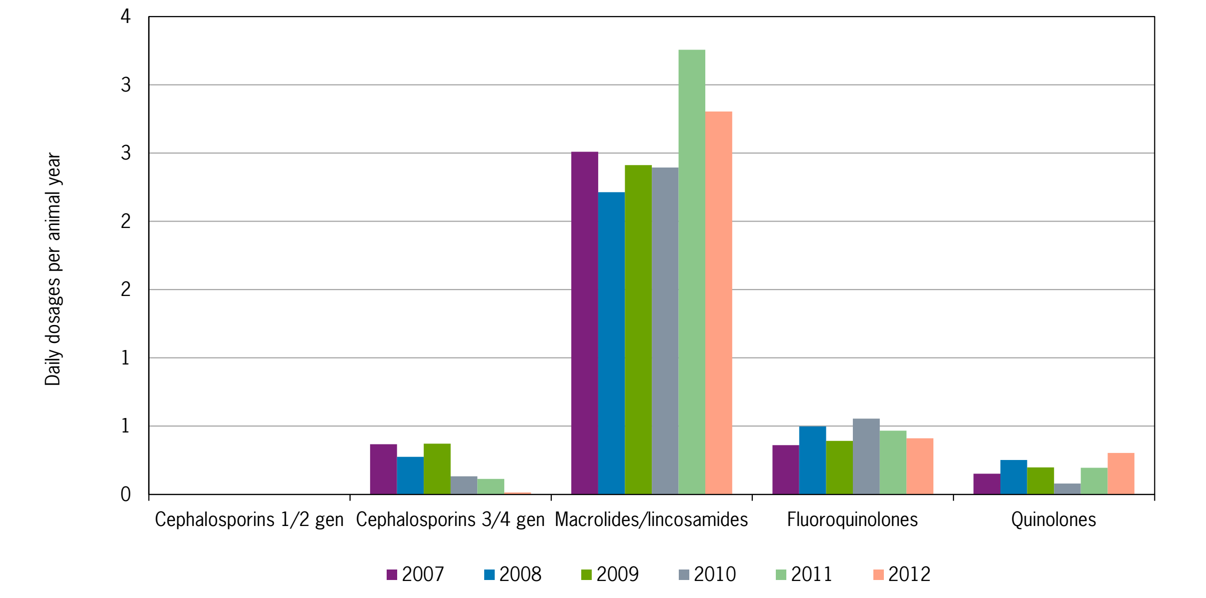


a) Results for 2012 are estimates, based on preliminary data of the first half year.

In 2012, 49% of the total antibiotic use on the veal calf farms originated from the administration of tetracyclines, 13% from macrolides/lincosamides, 10% from intestinal anti-infectives (e.g. neomycin, colistin) and 9% from trimethoprim/sulfonamides.

Figure 4.13 shows the trends in the use of the antimicrobial classes defined as the most critically important in human medicine by the World Health Organization i.e. third- and fourth-generation cephalosporins, fluoroquinolones and macrolides. The use of fluoroquinolones varies annually, with 1.9% of the total use in 2012. The use of third- and fourth-generation cephalosporins in veal calves decreased to almost zero (0.1%).

Figure 4.13	Antibiotic use in veal calves in dd per animal year, 2007-2012 a)



a) Results for 2012 are estimates, based on preliminary data of the first half year.

Discussion

Within the sample 31% of the veal calf farms had a use level within the target level ('streefniveau') for 2012 of the Animal Drug Authority (SDa, 2012), 50% within the signalling level ('signaleringsniveau'), and 19% within the action level ('actieniveau').

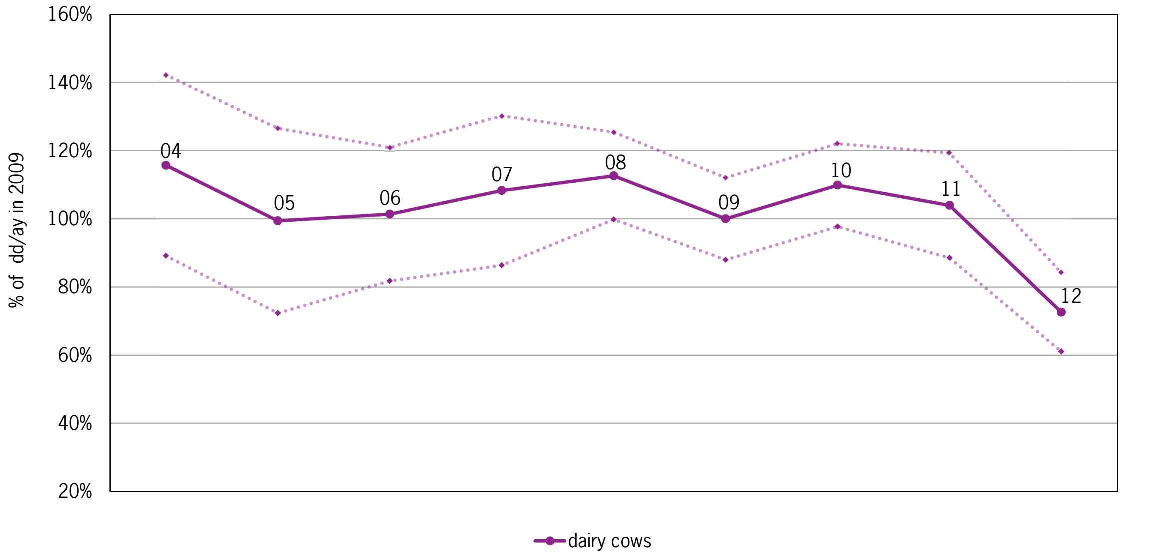
The overall use further decreased, mainly as a result of less use of traditional antibiotic therapy with tetracyclines. In 2012, 21 daily dosages of antibiotics were administered per animal year. This means that the individual average veal calf was treated with antibiotics during 13 days (= 21 x 222/365) in the period from birth (or more precisely: from arrival at the veal calf farm) to the average slaughter age of 222 days (white and rosé).

If it is assumed that the average treatment weight of veal calves is about 50% lower than the average live weight, since younger animals are more likely to receive antibiotics than older animals, the estimation of the true exposure during the total lifetime increases from 13 days to a total of 26 days.

4.4 Dairy cows

Figure 4.14 shows the trend in antibiotic use from 2004 to 2012: annual variation, strong decrease in 2012.

Figure 4.14 **Trends in antibiotic use in dairy cows, 2004-2012 a)**

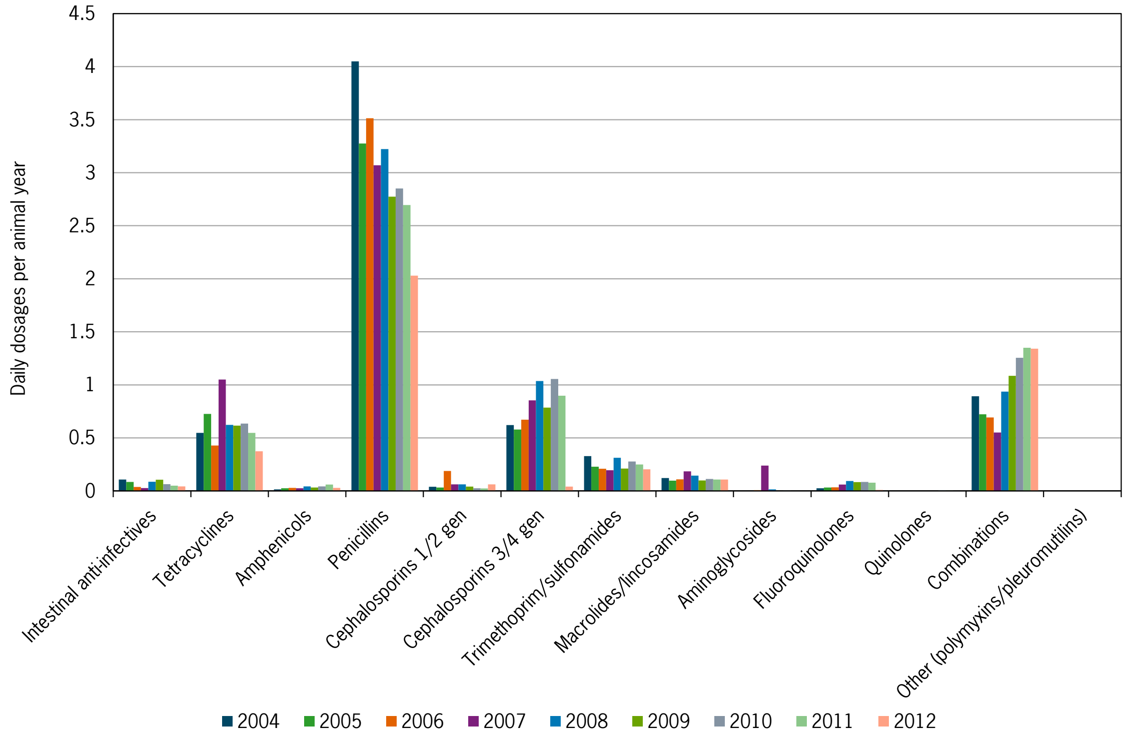


a) Results for 2012 are estimates, based on preliminary data of the first half year.

Based on the first semester, the average use in dairy cows is estimated to be 4.2 daily dosages per year in 2012, including the use in young stock (95% Confidence Interval: 3.6-4.9 dd/ay). In 2009 the use was 5.8 daily dosages per year (CI: 5.1-6.5 dd/ay).

Figure 4.15 provides insight into the trends in the relative use of the various groups of antibiotics.

Figure 4.15 **Antibiotic use in dairy cows in dd per animal year, 2004-2012 a)**

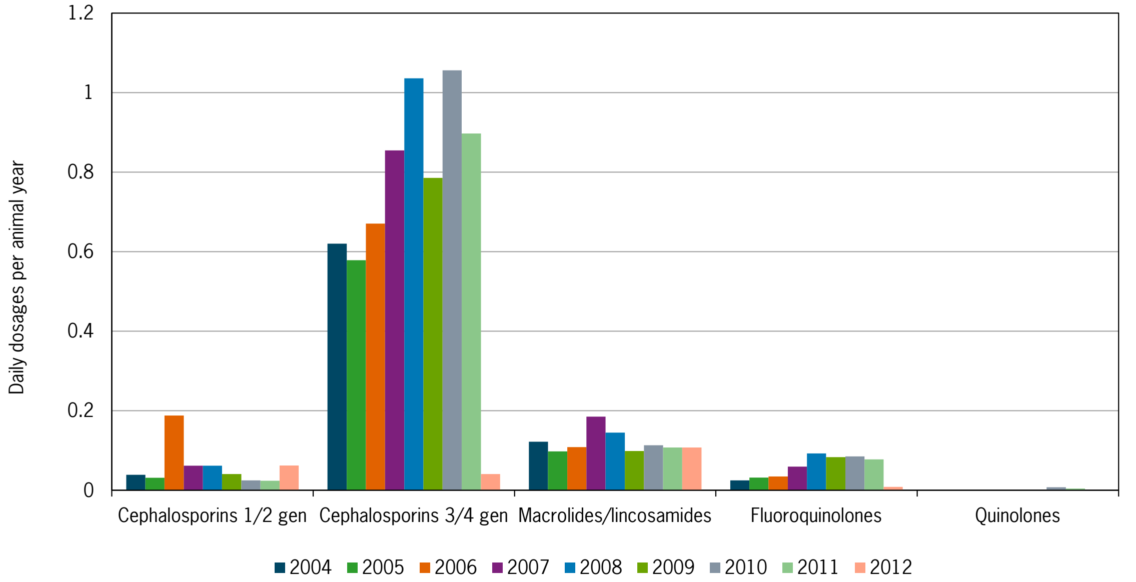


a) Results for 2012 are estimates, based on preliminary data of the first half year.

In 2012, 48% of the total antibiotic use on dairy farms originated from the administration of penicillins and 32% from combinations, which were mainly applications for intramammary treatment.

Figure 4.16 shows the trends in the use of the antimicrobial classes defined as the most critically important in human medicine by the World Health Organization, i.e. third- and fourth-generation cephalosporins, fluoroquinolones and macrolides. The use of third- and fourth-generation cephalosporins dropped from 13% in 2009 to almost zero (1%) in 2012. Furthermore, the use of fluoroquinolones in dairy cows showed a substantial decrease in 2009-2012 from 1.4% to 0.2%.

Figure 4.16	Antibiotic use in dairy cows in dd per animal year, 2004-2012 a)



a) Results for 2012 are estimates, based on preliminary data of the first half year.

Discussion

Within the sample about 62% of the farms had an antibiotic use within the target level ('streefniveau') for 2012 of the Animal Drug Authority (SDa, 2012), 29% between target value and signalling value, 7% above the signalling value ('signaleringswaarde'), and only one farm (less than 2%) above the action level ('actiewaarde').

In 2012 4.2 daily dosages of antibiotics were administered per animal year, of which 0.06 for oral use. If it is assumed that the oral use is only applied in young calves, an average calf is exposed to antibiotics during 2 days of the 56-day weaning period.

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Appendix

Table A.1 Trends in livestock in the Netherlands in number of animals (thousands)

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Piglets (less than 20 kg)	4,791	4,935	4,422	4,225	3,896	4,300	4,170	4,470	4,680	4,555	4,809	4,649	4,797
Sows	1,320	1,272	1,161	1,140	1,052	1,125	1,100	1,050	1,060	1,025	1,100	1,098	1,106
Fattening pigs (of at least 50 kg)	7,028	6,615	5,931	5,789	5,818	5,715	5,730	5,700	5,970	6,155	6,199	6,459	6,200
Turkeys	1,523	1,523	1,523	1,451	1,112	1,238	1,250	1,200	1,232	1,222	1,336	1,336	1,167
Other poultry	48,642	48,642	48,642	48,714	43,168	44,427	45,800	45,475	45,068	46,976	48,885	48,885	48,715
Veal calves	800	756	676	692	748	775	813	824	860	913	886	921	919
Cattle (excl. veal calves)	3,297	3,134	3,166	3,088	2,986	2,984	2,933	2,849	2,960	3,083	3,112	3,039	2,993
Sheep	1,152	1,250	1,250	1,300	1,476	1,700	1,725	1,755	1,715	1,545	1,091	1,211	1,113

Sources: Eurostat (pigs, cattle, sheep, laying hens before 2008), FAO (other poultry), CBS (laying hens 2008-2011);
FAO Poultry figures 2011 were not yet available; poultry numbers 2010 were used

Table A.2 Trends in livestock in the Netherlands in live weight (in 1,000 tonnes)

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Pigs	831	793	716	699	679	692	686	676	699	703	725	741	726
Turkeys	9	9	9	9	7	7	8	7	7	7	8	8	7
Other poultry	49	49	49	49	43	44	46	45	45	47	49	49	49
Veal calves	138	130	117	119	129	134	140	142	148	157	153	159	158
Cattle (excl. veal calves)	1,649	1,567	1,583	1,544	1,493	1,492	1,467	1,425	1,480	1,542	1,556	1,520	1,497
Sheep	69	75	75	78	89	102	104	105	103	93	65	73	67
Total	2,745	2,623	2,548	2,498	2,439	2,471	2,449	2,400	2,483	2,549	2,556	2,549	2,504

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