

# Consumption of drugs for sea lice infestations in Norwegian fish farms: methods for assessment of treatment patterns and treatment rate

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**ABSTRACT:** Sea lice are a major problem in Norwegian fish farms; however, data on drug treatment patterns or treatment rates of sea lice infestations are not available. Such data are important for analysing resistance patterns against drugs used for such infestations. The main objective of the present study was to develop a method to estimate the treatment patterns and treatment rates for drugs used in the treatment against sea lice (*Lepeophtheirus salmonis* and *Caligus elongatus*) in farm salmonids by means of national sales statistics. Annual sales figures, as weight of active substances, were obtained from the drug wholesalers and the feed mills. The weight of active drug substances is not useful as a unit of measurement of drug use in an epidemiological context because it does not correct for dosage differences and number of repeat treatments. To correct for these factors, we introduced approved daily dose ( $ADD_{\text{farm fish}}$ ) and treatment course-doses $_{\text{farm fish}}$   $\text{kg}^{-1}$  live-weight fish. To express the drug treatment patterns, the biomass (in weight) of farm salmonids treated with 1 course of a drug were estimated. When measured as kg active substance, the quantities of drugs for the treatment of sea lice infestations declined by 98% during the study period (1989 to 2002) but this figure increased 5-fold when it was corrected for differences in dosage. To correct for amounts of farm salmonids liable to require treatment we estimated the annual treatment rate, defined as the number of treatments for sea lice infestations per biomass slaughtered Atlantic salmon *Salmo salar* and rainbow trout *Oncorhynchus mykiss*. The annual treatment rate increased gradually during the study period; however, it varied considerably (range 0.45 to 1.34, mean 0.90). Before 1995, organophosphates were the most frequently used drugs against sea lice; since then pyrethroids have become the dominating drug group.

**KEY WORDS:** Sea lice · Drug use · Course-dose · Treatment patterns · Treatment rates

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## INTRODUCTION

Sea lice (*Lepeophtheirus salmonis*, also referred to as 'the salmon louse', and *Caligus elongatus*) are marine ectoparasitic copepods (Copepoda: Caligidae) on salmonid fishes. These parasites cause severe problems in the marine aquaculture of salmonids such as Atlantic salmon *Salmo salar* and rainbow trout *Oncorhynchus mykiss* in Northern Europe and on both coasts of North America. The parasites undergo 10 develop-

mental stages during their life period, each separated by a moult. The first 2 stages are planktonic, while the third, the copepodite, attaches to the fish. The next 4 stages (chalimus) are attached to the fish-host by a protein filament, while the last 3 (pre-adults and adult) can move freely on the surface of the host. These are often referred to as 'mobiles' and are the stages that cause problems for the host. Heavy sea lice infestations may cause primary (e.g. high levels of the stress hormone cortisol), secondary (e.g. osmoregulatory prob-

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lems) and tertiary (e.g. increased disease incidence) stress responses in salmonids (Grimnes & Jakobsen 1996, Bowers et al. 2000, Finstad et al. 2000, Mustafa et al. 2000). Infestation is controlled by management strategies (e.g. separation of year classes) and drug treatment.

Although sea lice infestations are a major problem in Norwegian fish farms, data on drug treatment patterns or on the treatment rates of sea lice infestations are not available. Such data are important for analysing resistance patterns against drugs used for the treatment of sea lice infestations. However, data on the consumption (as weight of active substance) of drugs used for sea lice infestations in Norway have been recorded and have been publicly available since 1981 (Grave et al. 1991). Because drugs formulated for use against sea lice infestations in farm salmonids are highly species-specific, national sales data of this drug group are thought to be a good estimate of the quantities used in this group. But weight of active substance as a unit of measurement does not take into account differences in the dose (differences in potency and bioavailability etc.) used for the various drug substances. This unit is therefore not useful when analysing and interpreting drug sales statistics in an epidemiological context, e.g. to estimate treatment patterns. Furthermore, to estimate the treatment rates of salmon lice infections, the population of farm salmonids liable to require treatment has to be considered. The main objective of this study was to develop a method to estimate treatment patterns and treatment rates of drugs used against sea lice infestations in farm fishes for human consumption, by use of national sales statistics.

## MATERIALS AND METHODS

**Data sources.** All drugs used for the treatment of farm fishes in Norway are prescription drugs. In addition to the preparations approved in Norway, veterinary surgeons may apply for authorisation to use drugs on farm fishes for which no marketing authorisation has been granted. All veterinary drugs have to be dispensed through pharmacies supplied solely by authorised drug wholesalers. An exemption is made for medicated feed for therapeutic use that is produced and dispensed by approved feed mills in accordance with EU directive 90/167/EEC.

Until 1999, overall sales data from the Norwegian drug wholesalers and feed mills dispensing medicated feed for therapeutic use in farm fishes were collected by the state-owned drug wholesaler Norwegian Medicinal Depot AS (NMD). From 1 January 2000, it has been mandatory for the drug wholesalers and feed mills dispensing medicated feed to report annual sales

figures to the Norwegian Institute of Public Health (NIPH). The annual sales figures, as kg active substance, for drugs used for sea lice infestations were provided for 1989 to 1999 by NMD, and for 2000 to 2002 by NIPH. The figures also include medicinal products exempted from market authorisation that are stocked on a regular basis by the drug wholesalers. For the year 1999, the sales data presented are incomplete because 1 wholesaler did not report all data (I. Litelskare unpubl. data). Because overall sales figures of drugs from the wholesalers and the feed mills roughly represent the quantities used of these drugs, the terms 'consumption' and 'usage' will be considered synonymous with 'sales figures' in this paper.

**Drug classification system.** In Norway, the Anatomical Therapeutic Chemical veterinary (ATCvet) classification system is used to classify veterinary medicinal products (WHO 2003a). The data presented in this study are classified according to the ATCvet classification system.

**Units of measurement for drug use.** In human medicine, defined daily doses (DDDs) are assigned by the WHO International Working Group for Drug Statistics Methodology (WHO 2003b) and the established DDDs are a consensus based on dosages approved in various countries. The DDD is used as a unit of measurement in drug-consumption studies, allowing comparison of drug use in a medical context, and also between periods, regions and countries (Capellà 1993, WHO 2003b). For drugs used on a short-term basis, the total treatment course dose (hereafter 'course-dose') may be used as unit of measurement (WHO 2003b).

Official DDDs have not been assigned for veterinary drugs. Therefore, in order to facilitate comparison of annual treatment patterns and treatment rates of drugs used for sea lice infestations we introduced approved daily dose ( $ADD_{\text{farm fish}}$ ) and treatment course-doses<sub>farm fish</sub> (in mg active substance) as a measurement unit for this group of drugs. The  $ADD_{\text{farm fish}}$  and course-doses<sub>farm fish</sub> are expressed per kg live-weight and are estimated on the basis of the approved dosages published by the Norwegian Compendium of Veterinary Medicines (Tørisen 1988–2002). These are 'pocket formularies' used by veterinary surgeons in their everyday practice, and contain the approved dosage recommendations for all pharmaceutical specialties with marketing authorisation in Norway. For drugs under exemption from market authorisation, we took the approved dosages given on the relevant package leaflets. The  $ADD_{\text{farm fish}}$  and the course-dose<sub>farm fish</sub> are thought to be close to the actual daily doses and course-doses used in practice. For drugs with a temperature-dependent dosage regimen, we selected the average of the dosage regimen representing a temperature range of 5 to 15°C as the  $ADD_{\text{farm fish}}$ .

Drugs used for sea lice infestation are either administered orally in the feed (over 7 to 14 d) or topically as a bath treatment. Some of the drugs administered as bath treatment have to be applied twice at 2 to 3 wk intervals to achieve optimal efficacy. For the orally administered drugs (QP53BC, QP54AA), we obtained the ADDs and the course-doses directly from the Norwegian Compendium of Veterinary Medicines. For the bath treatments (QP53AC, QP53AF) it was anticipated that 1 m<sup>3</sup> of delousing solution would be enough for a single bath treatment of 50 kg fish (0.02 m<sup>3</sup> kg<sup>-1</sup>). The ADD<sub>farm fish</sub> kg<sup>-1</sup> live-weight was estimated as the amount of drug (mg) recommended for 0.02 m<sup>3</sup> prepared delousing solution (Tørisen 1988–2002). The course-doses<sub>farm fish</sub> were set by multiplying the ADDs<sub>farm fish</sub> by the recommended number of repeated treatments per course for the relevant drug (Table 1).

**Treatment patterns.** The drug sales statistics (provided by NMD and NIPH) are expressed as kg active substance. The overall biomass (kg) of farm fishes treated annually with 1 course of a drug for sea lice infestations was estimated using the following formula:

$$\text{kg farm fishes treated} = \frac{\text{Amount (mg) of drug sold yr}^{-1}}{\text{Course-dose (mg) kg}^{-1} \text{ farm fish}}$$

**Annual treatment rate.** Because data on numbers of individuals liable to require treatment are not available, the biomass (kg) of salmonids slaughtered annually, was defined as the population liable to require

treatment for sea lice infestations. The annual treatment rate was defined as the calculated numbers of treatments for sea lice infestations per tonne Atlantic salmon and rainbow trout slaughtered each year (cumulative treatment rate). Data on the annual biomass of farm Atlantic salmon and rainbow trout slaughtered (for sale) for the years 1989 to 2000 were obtained from Statistics Norway (available at www.ssb.no 26 April 2004). The corresponding data for 2001 and 2002 were obtained from the Directorate of Fisheries (www.fiskeridir.no/sider/statistikk/opdrett/mat\_historie.xls 26 April 2004). The figures for 1991 have not been published since they were considered unreliable (www.ssb.no/aarbok/1996/tabeller/t351.html 26 April 2004).

**Number of fishes treated annually.** The estimated weight of farm Atlantic salmon and rainbow trout treated against sea lice does not give any information on the numbers treated (i.e. population liable to require treatment). In order to support the control of pharmaceutical residues in fish products, a national surveillance programme was established in Norway in January 1989 (Bangen et al. 1994). This programme requires that copies of all prescriptions for drugs intended for use on farm fishes be sent to the Directorate of Fisheries (DF), both by the prescribing veterinary surgeons and by the dispensing pharmacies and feed mills. Moreover, veterinary surgeons are obliged to fill out an authorised prescription form supplying fish-farm identity and locality, type and amount of the

Table 1. Dosage regimens, estimated ADDs<sub>farm fish</sub> (approved daily dosage) and course-doses<sub>farm fish</sub> for drugs used for the treatment of sea lice (*Lepeophtheirus salmonis* and *Caligus elongates*) infestations in farmed Atlantic salmon *Salmon salar* and rainbow trout *Onchorynchus mykiss* in Norwegian fish farms (Tørisen 1988–2002). ATCvet code: Anatomical Therapeutic Chemical veterinary classification system

| Drug group/<br>ATCvet code  | Active<br>substance              | Recommended dosage<br>per treatment (route of<br>administration) | Estimated<br>ADD <sub>farm fish</sub><br>(mg kg <sup>-1</sup> ) | Recommended<br>no. of<br>treatments | Estimated course-<br>dose <sub>farm fish</sub><br>(mg kg <sup>-1</sup> ) |
|---|----------------------------------|--|---|-------------------------------------|--|
| <b>Pyrethrins and pyrethroids</b>   |                                  |  |   |                                     |  |
| QP53AC01  | Pyrethrins <sup>a</sup>          | 100 mg m <sup>-3</sup> (bath)                                    | 2   | 1                                   | 2  |
| QP53AC08  | Cypermethrin                     | 5 mg m <sup>-3</sup> (bath)                                      | 0.1   | 1                                   | 0.1  |
| QP53AC08  | High- <i>cis</i> cypermethrin    | 15 mg m <sup>-3</sup> (bath)                                     | 0.3   | 1                                   | 0.3  |
| QP53AC11  | Deltamethrin                     | 3 mg m <sup>-3</sup> (bath)                                      | 0.06  | 1                                   | 0.06   |
| <b>Organophosphorous compounds</b>  |                                  |  |   |                                     |  |
| QP53AF17  | Azamethiphos                     | 100 mg m <sup>-3</sup> (bath)                                    | 2   | 2                                   | 4  |
| QP53AF02  | Metriphionate                    | 73 000 mg m <sup>-3</sup> (bath)                                 | 1460  | 2                                   | 2920   |
| QP53AF04  | Dichlorvos                       | 1000 mg m <sup>-3</sup> (bath)                                   | 20  | 2                                   | 40   |
| <b>Chitin-synthesis inhibitors</b>  |                                  |  |   |                                     |  |
| QP53BC02  | Diflubenzuron                    | 3 mg kg <sup>-1</sup> (oral)                                     | 3   | 14 d continuous                     | 42   |
| QP53BC03  | Teflubenzuron                    | 10 mg kg <sup>-1</sup> (oral)                                    | 10  | 7 d continuous                      | 70   |
| <b>Avermectins</b>  |                                  |  |   |                                     |  |
| QP54AA06  | Emamectin benzoate               | 0.05 mg kg <sup>-1</sup> (oral)                                  | 0.05  | 7 d continuous                      | 0.35   |
| <b>Other antiseptics and disinfectants</b>  |                                  |  |   |                                     |  |
|   | Hydrogen peroxide <sup>a,b</sup> | 1 500 000 mg m <sup>-3</sup> (bath)                              | 30 000  | 2                                   | 60 000   |
| <sup>a</sup> No specific dosage regimen recommended, values arbitrarily set; <sup>b</sup> ATCvet code not established |                                  |  |   |                                     |  |

drug prescribed, weight and species of fishes to be medicated, reason for the treatment (diagnosis), starting date of the treatment and recommended withdrawal periods. DF routinely computerises this information, creating a nationwide database for the status of drug treatment in Norwegian fish farms.

The average size of farm fishes treated with the different drugs against sea lice were estimated based on data from DF's database for the period 2000 to 2002. These years were selected because the data programme used by DF in these years allowed electronic conversion of the recorded data to a Microsoft® Excel spreadsheet, while a direct conversion was impossible for the prescription data of the preceding years. The data covering the period 1989 to 1999 (approx. 1500 prescriptions yr<sup>-1</sup>) would have to be repunched manually to obtain historical data for the whole period, and this could not be justified because of the labour cost.

Data on the average size of the farm fishes for each drug prescribed were used to estimate the number of fishes treated, since such data are not available in DF's database. The annual numbers of farm salmon and rainbow trout treated with the different drugs against sea lice for the years 2000 to 2002 was estimated by

No. of fishes treated per year with Drug X =

$$\frac{\text{Estimated biomass (kg) of fishes treated with Drug X yr}^{-1}}{\text{Average fish weight (kg) treated with Drug X yr}^{-1}}$$

## RESULTS

### Treatment patterns

The annual sales figure for drugs used for the treatment of sea lice infestation in the Norwegian fish-farming industry during the period 1989 to 2002 declined by 98 % when expressed as weight of active substances (Table 2).

The estimated biomass of farm Atlantic salmon and rainbow trout treated with 1 course against sea lice versus biomass slaughtered annually are shown in Fig. 1. These amounts (excluding 1991 and 1999 for which insufficient data were available) correlate well ( $r^2 = 0.980$ ). The calculated amounts of farm salmonids treated increased 5 times in the study period; however, great variation was found. The amount was lowest in 1993 and peaked in 2000, while in the period 2000 to 2002 a 2 % decrease was observed.

In the period 1989 to 1992, only organophosphorous compounds were used to combat sea lice infestations in Norwegian fish farming. From 1992, new drugs against these parasites were introduced, and the treatment patterns of drugs against sea lice gradually changed. Drugs belonging to the pyrethroid group were introduced in 1994; 2 yr later the proportion of farm fishes (biomass) treated with a drug from the pyrethroid group was on average 58 %. In 2002, this figure was 91 %, while for the avermectins the corresponding figure was 9 %.

Table 2. Sales figures (in kg active substances) of drugs used for the treatment against sea lice (*Lepeophtheirus salmonis* and *Caligus elongatus*) infestations in farmed Atlantic salmon *Salmon salar* and rainbow trout *Onchorhynchus mykiss* in Norwegian fish farms. Data are based on sales from feed mills and drug wholesalers. ATCvet code: Anatomical Therapeutic Chemical veterinary classification system

| Drug group/<br>ATCvet code                 | Active<br>substance              | 1989        | 1990        | 1991        | 1992        | 1993        | 1994        | 1995        | 1996        | 1997        | 1998        | 1999 <sup>a</sup> | 2000       | 2001       | 2002       |
|--|----------------------------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|-------------------|------------|------------|------------|
| <b>Pyrethrins and pyrethroids</b>          |                                  |             |             |             |             |             |             |             |             |             |             |                   |            |            |            |
| QP53AC01                                   | Pyrethrins                       |             |             |             |             |             | 32          | 26          | 9           | 18          |             |                   |            |            |            |
| QP53AC08                                   | Cypermethrin                     |             |             |             |             |             |             |             | 23          | 28          | 3           | <0.1              | <0.1       |            |            |
| QP53AC08                                   | High- <i>cis</i> cypermethrin    |             |             |             |             |             |             |             |             |             |             | 19                | 73         | 69         | 62         |
| QP53AC11                                   | Deltamethrin                     |             |             |             |             |             |             |             |             |             | 19          | 11                | 23         | 19         | 23         |
| <b>Organophosphorous compounds</b>         |                                  |             |             |             |             |             |             |             |             |             |             |                   |            |            |            |
| QP53AF17                                   | Azamethiphos                     |             |             |             |             |             | 389         | 738         | 606         | 315         | 182         | 14                |            |            |            |
| QP53AF02                                   | Metriphonate                     | 3300        | 2408        | 2144        | 1946        | 1779        | 1227        | 281         | 138         |             |             |                   |            |            |            |
| QP53AF04                                   | Dichlorvos                       | 3488        | 3416        | 3588        | 3115        | 2470        | 1147        | 395         | 161         | 36          |             |                   |            |            |            |
| <b>Chitin-synthesis inhibitors</b>         |                                  |             |             |             |             |             |             |             |             |             |             |                   |            |            |            |
| QP53BC02                                   | Diflubenzuron                    |             |             |             |             |             |             |             | 160         | 361         | 437         | 50                | 12         |            |            |
| QP53BC03                                   | Teflubenzuron                    |             |             |             |             |             |             |             | 610         | 1510        | 1334        | 231               | 62         | 28         |            |
| <b>Avermectins</b>                         |                                  |             |             |             |             |             |             |             |             |             |             |                   |            |            |            |
| QP54AA06                                   | Emamectin benzoate               |             |             |             |             |             |             |             |             |             |             | 4                 | 11         | 12         | 20         |
| <b>Total in kg</b>                         |                                  | <b>6788</b> | <b>5824</b> | <b>5732</b> | <b>5061</b> | <b>4249</b> | <b>2795</b> | <b>1440</b> | <b>1707</b> | <b>2268</b> | <b>1975</b> | <b>329</b>        | <b>181</b> | <b>128</b> | <b>105</b> |
| <b>Other antiseptics and disinfectants</b> |                                  |             |             |             |             |             |             |             |             |             |             |                   |            |            |            |
|  | Hydrogen peroxide <sup>b,c</sup> |             |             |             |             | 710         | 290         | 340         | 160         | 200         |             |                   |            |            |            |
| <b>Total in tonnes</b>                     |                                  |             |             |             |             | <b>710</b>  | <b>290</b>  | <b>340</b>  | <b>160</b>  | <b>200</b>  |             |                   |            |            |            |

<sup>a</sup>Data incomplete for 1999 because 1 wholesaler failed to report all sales; <sup>b</sup>ATCvet code not established; <sup>c</sup>sales figures given in tonnes

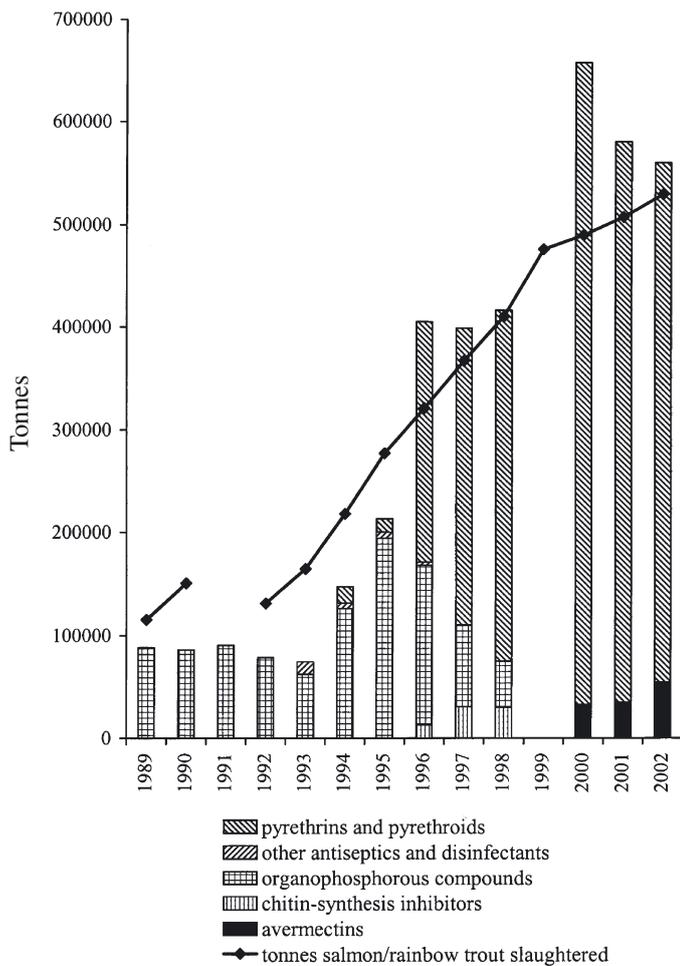


Fig. 1. Estimated overall biomass of farm Atlantic salmon *Salmo salar* and rainbow trout *Oncorhynchus mykiss* in Norwegian fish farms treated annually with 1 treatment course (calculated as mg of Drug X sold  $\text{yr}^{-1}$  / course-dose (mg)  $\text{kg}^{-1}$  fish) against sea lice (*Lepeophtheirus salmonis* and *Caligus elongatus*) (data for 1999 omitted since incomplete), expressed as tonnes treated versus tonnes slaughtered (data for 1991 omitted since unreliable)

#### Estimated annual treatment rate

The estimated treatment rate against sea lice varied considerably, but increased by 37% from 1989 to 2002 (Fig. 2). The treatment rate was lowest in 1993 and peaked in 2000 (range 0.45 to 1.34, mean 0.90).

#### Estimated size and numbers of farm fishes treated

DF's prescription database contained information on 6530 drug prescriptions for treatment against sea lice for the years 2000 to 2002. A total of 5244 (80%) of these prescriptions included information on the size of the fish to be treated. Of the prescriptions giving

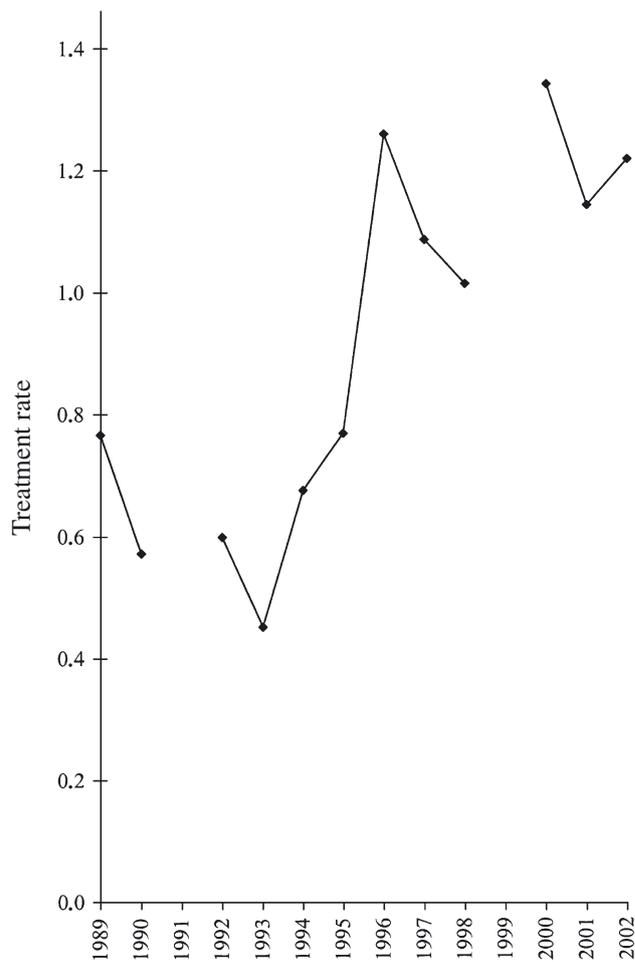


Fig. 2. Estimated annual treatment rate of sea lice infestations (*Lepeophtheirus salmonis* and *Caligus elongatus*) in farm Atlantic salmon *Salmo salar* and rainbow trout *Oncorhynchus mykiss* in Norwegian fish farms (sales data for 1999 were incomplete; data for biomass of farm salmonids for 1991 were unreliable)

information on fish size, we excluded 161 for farm Atlantic salmon or rainbow trout weighing  $>5$  kg (mean weight 6.7 kg; range 5.1 to 15 kg) because these mainly represented brood stock not intended for human consumption. The annual average size of the farm fishes treated against sea lice with the drugs included were calculated based on data from 5083 prescriptions (Table 3). The figures show that the average weight of fishes treated with high-cis-cypermethrin and deltamethrin varied within a range of less than 7% from 2000 to 2002 (2.40 to 2.58 kg). The average weight (mean value) of fishes treated with emamectin benzoate increased by 33% from 0.35 to 0.52 kg in the same period. The average weight of fishes treated with the chitin-synthesis inhibitor teflubenzuron was approximately the same (1 kg) in 2000 and 2001.

Table 3. The annual average size (in kg) of farmed Atlantic salmon *Salmon salar* and rainbow trout *Onchorynchus mykiss* in Norwegian fish farms treated with the various drugs against sea lice (*Lepeophtheirus salmonis* and *Caligus elongates*) during 2000–2002. Data were derived from Directorate of Fisheries' prescription database (N = 5083). ATCvet code: Anatomical Therapeutic Chemical veterinary classification system. n: number; CI: confidence interval

| Drug group/ATCvet code             | Active substance              | 2000<br>kg (95% CI)/n | 2001<br>kg (95% CI)/n | 2002<br>kg (95% CI)/n |
|------------------------------------|-------------------------------|-----------------------|-----------------------|-----------------------|
| <b>Pyrethrins and pyrethroids</b>  |                               |                       |                       |                       |
| QP53AC08                           | Cypermethrin                  | 1.03 (CI not)/2       | –                     | –                     |
| QP53AC08                           | High- <i>cis</i> cypermethrin | 2.46 (2.32–2.59)/473  | 2.55 (2.41–2.690)/372 | 2.58 (2.46–2.70)/367  |
| QP53AC11                           | Deltamethrin                  | 2.43 (2.34–2.52)/853  | 2.56 (2.47–2.65)/769  | 2.40 (2.31–2.49)/697  |
| <b>Chitin-synthesis inhibitors</b> |                               |                       |                       |                       |
| QP53BC02                           | Diflubenzuron                 | 0.3 (CI not)/4        | –                     | –                     |
| QP53BC03                           | Teflubenzuron                 | 0.98 (CI not)/5       | 1.01 (CI not)/5       | –                     |
| <b>Avermectins</b>                 |                               |                       |                       |                       |
| QP54AA06                           | Emamectin benzoate            | 0.35 (0.32–0.38)/446  | 0.35 (0.32–0.38)/520  | 0.52 (0.46–0.58)/570  |

The estimated annual numbers of farm Atlantic salmon and rainbow trout treated with 1 course against sea lice during 2000 to 2002 are presented in Fig. 3. The numbers declined by 11% from 2000 to 2002. Measured as number of fishes treated with the different drug groups, the estimated proportion of farm Atlantic salmon and rainbow trout (in numbers) treated with a drug belonging to the avermectins was 26% in 2000, increasing to 34% in 2002. The corresponding figures for the pyrethroid group were 74 and 66%, respectively. The calculated proportion (in numbers) of farm fish treated with chitin-synthesis inhibitors was 0.5, 0.1 and 0% in 2000, 2001 and 2002, respectively.

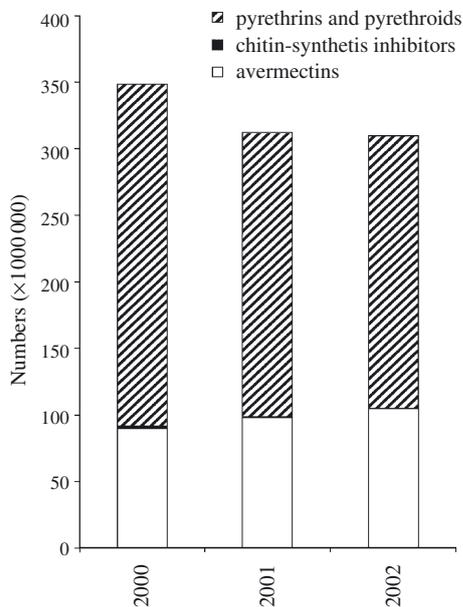


Fig. 3. Estimated numbers of farm Atlantic salmon *Salmo salar* and rainbow trout *Oncorhynchus mykiss* treated with 1 treatment with different drugs against sea lice (*Lepeophtheirus salmonis* and *Caligus elongates*) infestation in Norwegian fish farms

## DISCUSSION

### Data sources

Several studies have concluded that the data provided by the wholesalers and the feed mills on the sales of drugs for the treatment of farm fishes in Norway are nearly identical with the corresponding data derived from prescriptions (Bangen et al. 1994, Grave et al. 1999, 2002). Furthermore, of the 6530 prescriptions in DF's database for drugs indicated for use against sea lice, all but 3 were for Atlantic salmon or rainbow trout. Thus, the sales figures included in this study give reliable data on the consumption of drugs against sea lice by salmonids in Norwegian fish farms.

The prescription database of the DF contains almost all prescriptions issued for use on farm fishes in Norway (Bangen et al. 1994, Grave et al. 2003). On average, 80% of the prescriptions covering the years 2000 to 2002 gave information on fish size. Therefore, the estimated fish sizes used in the present study to calculate the number of farm fishes treated with the different drugs are considered representative estimates.

### Treatment patterns

The relative use of different agents against sea lice changed considerably from 1989 to 2002, as evident from Fig. 1. Until the mid-1990s, almost all treatments were performed with organophosphates. Mefenoxate (trichlorfon), a weak inhibitor of cholinesterases, was introduced in 1974 for the treatment of sea lice infestations in the Norwegian fish-farming industry. In 1986, the cholinesterase inhibitor dichlorvos was introduced. Organophosphorous drugs were the drugs of choice for the treatment of sea lice infestations during the period 1981 to 1988 also (Grave et al. 1991).

Treatments with drugs of the pyrethrin/pyrethroid group were introduced in 1990 (Jakobsen & Holm 1990), but no significant use was recorded before 1994. The first product available was based on pyrethrum, a mixture of 6 compounds with antiparasitic properties (pyrethrins), extracted from the plant *Chrysanthemum cinerariaefolium*. The proposed application method for this compound, a surface layer of a pyrethrum-oil mixture in the net-pen, was impracticable, and synthetic compounds administered as a bath treatment soon replaced this drug (Hart et al. 1997). In 1996, a cypermethrin product with an equal mix of the cis and trans isomers was introduced. In 1998, a product containing deltamethrin was introduced, shortening the treatment time from 60 to 30 min. The original cypermethrin product was replaced in 1999 by a product containing a higher proportion of the more effective cis-isomers, with a recommended treatment time of 30 min. In the period 1993 to 1997, hydrogen peroxide was used to some extent, mainly due to development of resistance against organophosphates in a few areas (Denholm et al. 2002). A relatively narrow margin of safety combined with a moderate efficacy (Bruno & Raynard 1994, Treasurer & Grant 1997) resulted in a short lifespan of this product.

In the period 1996 to 2001, chitin-synthesis inhibitors were used as in-feed compounds, but this group of drugs did not gain a big share of the market. In 1999, the avermectin emamectin benzoate was introduced, also as an in-feed product, and offered an effective alternative to the labour-intensive bath treatments (Stone et al. 2000). Emamectin benzoate could initially only be used on small fish, due to a withdrawal period of 120 d (independent of temperature). The withdrawal period (the period between the last day of treatment and the first day on which the fishes can be harvested) is a major factor of consideration when choosing a drug for treatment. A long quarantine period makes it impossible to slaughter fishes in case of emergencies (e.g. algal blooms), and is an important factor to consider when choosing a drug for the treatment of fishes close to market size. In 2002, the withdrawal period was recalculated on the basis of the maximum residues limit (MRL-value) for all drugs used in the treatment of aquatic organisms (Directorate of Fisheries 2003). This changed the withdrawal period for emamectin benzoate to 175 ( $^{\circ}\text{C}$ ) days (temperature  $\times$  days). A withdrawal time of 120 d thus represents a temperature of 1.5 $^{\circ}\text{C}$ . Because treatments against sea lice are usually performed at much higher temperatures than 1.5 $^{\circ}\text{C}$ , since 2002 the withdrawal period has been substantially lowered for the majority of treatments with emamectin. Thus, the 33% increase in the weight of fishes treated with emamectin from 2000 to 2002 is likely to be a result of this change in the withdrawal

period. However, the predominant treatment for larger fishes (>1 kg) in 2002 was still pyrethroids, mainly because of the lower costs of these drugs when treating fish of larger size, and the possibility of being able to use these compounds up until 1 wk prior to slaughter. There was no variation in the average weight of fish treated with the chitin-synthesis inhibitor teflubenzuron between 2000 and 2001.

### Estimated annual treatment rate

Although considerable fluctuations were found, the present study has shown an increase in the annual treatment rate in the period 1989 to 2002 (Fig. 2.) These variations most probably reflect variations in sea lice infestation due to climatic variations between different years. Warm and sunny springs tend to boost the reproduction of sea lice, resulting in greater infestations than in colder springs. This may have caused higher numbers of re-infections in some farms and may explain why the annual treatment rate (actual cumulative treatment rate) peaked in 1996, 2000 and 2002.

There may be several explanations for the observed increase in the annual treatment rate over the years. Until the mid-1990s, organophosphorous drugs dominated as sea lice agents. These compounds have a limited efficacy on the chalimus stages of the parasite, and are recommended to be used twice within a 14 d period in order to obtain optimal efficacy (Tørisen 1988–2002). This treatment protocol may not always have been followed. Bath treatments against sea lice are labour-intensive procedures, and it is believed that when using organophosphorous drugs, some fish-farmers did not comply with the recommendation to repeat the treatment. Thus, the course-doses<sub>farm fish</sub> for this drug group may be too high, resulting in an underestimation of the annual treatment rate for this drug group. This may explain why the estimated treatment rate was substantially lower for the period 1989 to 1995 (when organophosphates were the dominant drug group) than for the last part of the study period. As pyrethroids need only to be applied once to obtain the same treatment efficacy as organophosphates (Hart et al. 1997), we do not consider that the course-doses<sub>farm fish</sub> set for this drug group are confounded by non-compliance. The course-doses in the present study for pyrethroids are thought to be good estimates.

Another factor contributing to an increase in the annual treatment rate in the last part of the study period was a tendency by farmers during this period to initiate treatments at lower numbers of sea lice per fish. In 1997, a national programme for the control of sea lice was introduced in Norway. The main purpose was to keep the number of parasites as low as possible

in the spring, when wild salmon smolts from the rivers head for the sea and pass through the farming areas. In the period 1997 to 1999, this programme was organised on a regional basis, while from 2000 onwards it was organised on a national level. From 2000 onwards, the maximum number of *Lepeophtheirus salmonis* allowed on each fish during the migration period of wild salmon smolts was 0.5 adult females, or 5 mobiles (sum of all post-chalimus stages). Sea lice numbers were recorded twice a month, and if a higher average number was found, a drug treatment was mandatory; non-compliance with these recommendations could result in considerable fines (Ministry of Agriculture 2000).

Lastly, the introduction of effective oral products such as emamectin benzoate lowered labour costs substantially and thus the trigger point for treatment.

Although the biomass of fishes slaughtered each year does not accurately represent the biomass in the net-pens throughout the year, it is considered to be a good estimate. Since farm fishes gain weight continuously until slaughter, the biomass of live individuals in the net-pens will always be slightly lower than the slaughtered biomass. Our calculations may therefore overestimate biomass and thus underestimate treatment rate. Biomass is thought to be a good estimate of the population liable to require treatment if the average size of fish treated with a specific drug is stable, and may enable comparable estimates of the treatment rate between periods (years). For the period 1989 to 2001, there were no obvious factors (e.g. changes in withdrawal periods) that would have influenced size of treated fishes. In the present study, the average weight of fishes treated with emamectin benzoate increased by 33% from 2000/2001 to 2002. When the average size of treated fishes increases, then the number of individuals that can be treated with a certain quantity of a drug decreases. Consequently, the population liable to require treatment measured as the biomass (of farm fishes) is an overestimate for emamectin benzoate for 2002 compared with the other years, and the estimated treatment rate for this year is underestimated. Because emamectin benzoate comprised only a minor proportion of the treatments in 2002, the underestimate is not of statistical significance.

## CONCLUSIONS

When consumption of drugs against sea lice was expressed as weight of active substances, a 98% decrease was observed for the period 1989 to 2002. However, when expressed as annual treatment rate, the usage increased by 37% during the study period. It is concluded that in order to evaluate the prescription

patterns of drugs against salmon lice infestations, it is crucial to correct for differences in dosages and number of repeated treatments between the various drug substances. Although fish biomass does not provide information about population numbers liable to require treatment, it was found to be a useful denominator in estimating annual treatment rate. An exception is when there are large variations in the average weight of fishes treated with drugs that are frequently used.

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