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Outpatient antibiotic use in Ireland in the first half of 2009

Introduction

Surveillance of antimicrobial usage has been identified as a key component in the WHO Global Strategy of Containment of Antimicrobial Resistance and the Strategy for the control of Antimicrobial Resistance in Ireland (SARI). Ireland participates in the European Surveillance of Antimicrobial Consumption (EASC) project, which aims to construct an inventory of antibiotic usage in the EU at national level by collating data from both outpatient (primary care or community) and hospital care areas.

In an ESAC report of outpatient antibiotic consumption from 29 EU countries with reliable data for 2005, the range of outpatient antibiotic usage was 9.2 DID (Russian Federation) to 34.7 DID (Greece). The median for all countries was 18.1 DID.¹ Outpatient antibiotic usage in Ireland has been around 19 - 23 DID over the last five years. Thus the overall rate in Ireland is mid-to-high in Europe. Furthermore, the ESAC report also highlighted that Ireland was one of only four countries where the trend in consumption was increasing while six of the remaining 25 countries showed a decrease in usage.

The first-ever European Antibiotic Awareness Day (EAAD) took place across Europe on Tuesday 18th November 2008.² To mark the day, a seminar was held in Dublin to highlight initiatives being taken to combat over-use of antibiotics in Ireland and included:

- a media campaign
- an educational programme for General Practitioners
- development of antibiotic prescribing guidelines
- distribution of educational material through health centres and community pharmacies

The overall outpatient antibiotic consumption for Ireland in 2008 was 21.5 DID, a decrease from the previous year's rate of 22.4 DID, the first time the yearly trend has decreased since 2000.³ Furthermore, a significant decrease in antibiotic consumption was already seen for the month of November in 2008, however, a more detailed analysis of subsequent month's data is needed to quantify the effect of EAAD.

This work aims to provide a preliminary estimate of the extent of the impact of the November 2008 EAAD event on the Irish outpatient antibiotic consumption over the first half of 2009.

Methods

HPSC has purchased Irish antibiotic sales data from IMS Health, a pharmaceutical market research company. This dataset contains regional, monthly wholesaler to retail pharmacy sales data from over 95% of the wholesalers and manufacturers in Ireland. Consumption is measured in Defined Daily Dose (DDD), which is the assumed average maintenance dose per day for a drug used for its main indication in adults. An automated data-extraction protocol was devised at HPSC to obtain the DDD outputs for antibiotics. The current WHO Anatomical Therapeutic Chemical index was used to classify the antibiotics.⁴

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Rates were calculated in DDD per 1000 inhabitants per day (DID) for the outpatient antibiotic consumption data. Updated population size estimates were obtained from the Central Statistics Office⁵ and used to calculate monthly rates. Monthly expected usage values for 2000-2008 were calculated from time-series data using an exponential smoothing (Holt-Winters) model and projections were obtained for the first six months of 2009 using the same model.

Results

Preliminary estimates of overall outpatient antibiotic consumption for the first half of 2009 was 20.3 DID. This is a decrease from the overall 2008 figure of 21.5 DID. However, full-year to half-year comparisons are invalid as antimicrobial consumption behaviour in Ireland is highly seasonal. Analysis of the crude DDD figures shows that the amount of antibiotic drugs consumed in Ireland fell by 7.9% when compared to the first six months of 2008 (see table 1). Note that this measure does not take into account the changes in the underlying population.

Table 1. Total Defined Daily Doses (DDD) and the percent changes between consecutive first and second halves of each year.

	<i>January to June</i>		<i>July to December</i>	
	DDD	% Change	DDD	% Change
2000	11,761,025		12,375,194	
2001	13,273,785	12.9%	13,018,777	5.2%
2002	13,489,770	1.6%	13,677,692	5.1%
2003	14,317,647	6.1%	15,225,074	11.3%
2004	14,374,306	0.4%	15,582,021	2.3%
2005	15,635,395	8.8%	15,463,002	-0.8%
2006	17,389,301	11.2%	15,539,142	0.5%
2007	17,779,254	2.2%	17,756,769	14.3%
2008	17,762,362	-0.1%	17,030,781	-4.1%
2009	16,350,549	-7.9%		

A more detailed statistical analysis showed that, while for January of 2009 the rate of consumption was the highest ever seen in any single month, the average monthly consumption for the first half of 2009 fell by 12.6% (see figure 1). The model was fitted on the monthly time-series of 2000 to 2008 data and had a Mean Absolute Percentage Error (MAPE) of 5.5; that is, there was deviation in the observed data of about 5% either side of the predicted values. The MAPE for the six months in 2009 was 16.3 (see table 2) and the observed values for Feb-June are all lower than the lower 95% confidence intervals of the projected rates, showing that the trend in the rates for 2009 is significantly different from the historical trend.

Figure 1. Monthly antibiotic consumption rates in Ireland in Defined Daily Doses per 1000 Inhabitants per Day (blue points). An exponential smoothing model was established using 2000 to 2008 data (solid red line) and used to project forecast rates for the first half of 2009 (broken red line).

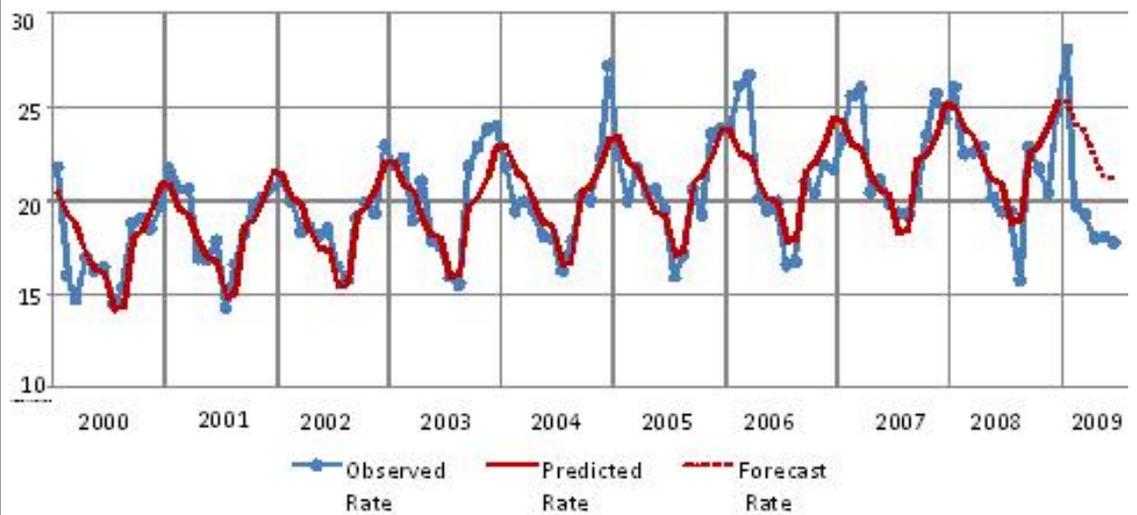


Table 2. Provisional results for outpatient antibiotic consumption in 2009 by month in Defined Daily Doses per 1000 Inhabitants per Day (DID). The projected values were derived from historical trends (see text for details) along with lower and upper 95% confidence intervals. Also shown are the deviations of the observed data from the project figures in DID and percentage.

Month in 2009	Observed DID (provisional)	Projected DID	Deviation from Observed in DID	Percent Deviation from Observed	Lower 95% Confidence Interval	Upper 95% Confidence Interval
January	28.1	25.3	2.8	11.0%	22.3	28.3
February	19.7	24.0	-4.3	-17.8%	21.1	27.0
March	19.3	23.7	-4.4	-18.6%	20.7	26.7
April	18.0	22.3	-4.3	-19.1%	19.3	25.3
May	18.1	21.4	-3.2	-15.1%	18.4	24.3
June	17.8	21.2	-3.4	-16.1%	18.2	24.2

Discussion

Previous analyses at the HPSC have highlighted important characteristics of outpatient antibiotic usage in Ireland. Usage in some counties appears to be considerably different from the national rate (17.4 to 27.9 DID in 2008). This regional variation is similar to the pattern seen since 2004, and may reflect differences in prescribing practices, socioeconomic factors or pharmaceutical marketing.⁶ Analysis of Primary Care Reimbursement data showed that those entitled to reimbursement (representing 30% of the population) are prescribed about 55% of the antibiotics in terms of cost. Seasonal fluctuation (26% rise in DID from summer to winter) has been seen every year in outpatient antibiotic consumption and is probably related to over-prescribing of antibiotics for respiratory tract infections in winter months. In a separate analysis of recent Irish data, it was shown that outpatient use of specific antibiotics is strongly associated with seasonal influenza activity.⁷ The three factors – regional, seasonal and socioeconomic – may work together to produce very high rates of antibiotic consumption in some primary care areas at certain times, resulting in increased pressure for selection of resistant variants of important bacterial pathogens.

The marked seasonal fluctuation coupled with a higher proportion of broad-spectrum penicillin consumption in Ireland is consistent with those countries having a higher level of resistance among key indicator pathogens, as in Portugal and Italy, unlike the Nordic countries, which generally have low levels of resistance. In Ireland proportion of invasive *Streptococcus pneumoniae* isolates that are penicillin non-susceptible has been steadily increasing and is currently at 26%.⁸ Furthermore, high-level penicillin resistance (6%) in invasive pneumococcal

isolates in Ireland is among the highest in Europe.

It is encouraging that all methods used to detect changes in outpatient antibiotic consumption in Ireland since the November 2008 EAAD event have indicated a decline. The modelling method which takes the difference between actual usage rates and those projected from historical data assuming no intervention had occurred, is probably the most robust technique applied. An estimated average monthly decrease of 12.6% produced in this manner includes the high peak in January of 2009. During that time, the seasonal influenza rate was the highest for the last nine years with the influenza-like illness (ILI) at over 200 consultations per 100,000 population, and it is likely that the high antimicrobial use was, at least partly, a result of inappropriate prescribing for viral infections. Antibiotic consumption rates for the other five months of 2009 were considerably lower than forecasted. It is estimated that even a 10% reduction in the average monthly consumption rates would result in a saving of €6 million over the year in ingredient costs alone to both private patients and to the reimbursement services. The benefits to public health in terms of reduction in antimicrobial resistance among pathogens such as *S. pneumoniae* will no doubt take more time to take effect.

The second European Antibiotic Awareness Day is planned to take place on 18th November 2009, with a similar set of events as the first day. However, with the ILI rate increasing again in autumn 2009 in Ireland, largely as a result of the circulating Pandemic Influenza A(H1N1), it remains to be seen if the interventions established since the first EAAD event will continue to have a positive impact.

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