Using defined daily doses to study the use of antibacterials in UK hospitals

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- OBJECTIVE — To explore the feasibility of using defined daily doses (DDDs) to measure antibacterial consumption in a UK hospital and identify the methodological issues encountered.
- DESIGN — Descriptive study.
- SUBJECTS AND SETTING — A London teaching trust, with four hospital sites and 1,000 beds.
- OUTCOME MEASURES — Total DDDs per 100 occupied bed days (OBD) for financial years 2002–03, 2003–04 and 2004–05; proportion of DDDs given intravenously and orally; usage by antibacterial class; comparison with UK and international data.
- RESULTS — Antibacterial consumption ranged from 85.5 to 91.5 DDDs per 100 OBD across the three years studied. The proportion of oral DDDs increased over the three-year period. The antibacterial groups with the highest consumption were penicillins and cephalosporins. A range of methodological issues were encountered, such as how to address medicines dispensed for discharge as part of a one-stop dispensing scheme, and other practical issues. Usage was in line with other UK sites, but higher than elsewhere in Europe.
- CONCLUSION — It is possible to obtain data on DDDs in the UK hospital setting, although a variety of methodological issues may need to be addressed. A standardised UK approach is needed, so that data obtained from different sites can be compared in a meaningful manner.

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Increasing resistance to antibacterials is a major public health problem. Antibacterial use is considered to be the main selective pressure driving this resistance,[1,2] and the rate at which resistance develops has been shown to be associated with drug consumption.[3] It has been suggested that reductions in the development of resistance will only result from significant changes in antibacterial use.[3] Despite the majority of antibacterial courses being prescribed in primary care, the prevalence of both antibacterial use and antibacterial resistance is higher in secondary care.[4] Surveillance of hospital use of antibacterials is therefore particularly important.

There are several ways in which antibacterial consumption can be assessed. In UK secondary care, expenditure is routinely used. However changes in pricing structure and the availability of generic medicines make it difficult to compare different organisations and different periods. Consumption can also be expressed in terms of numbers of packs dispensed, but this also has limitations as pack sizes vary both within and between institutions. The ideal way of monitoring consumption would be based on individual prescription data, but this will not be practical in UK hospitals until the widespread availability of electronic prescribing with appropriate reporting facilities. In the meantime, point prevalence studies have been used to study antibacterial use.[5] This method gives detailed information about prescribing but only at one point in time.

Outside the UK, the calculation of defined daily doses (DDDs) is widely used. The DDD is the assumed average maintenance dose per day for a drug when used for its main indication in adults with normal organ function. DDDs for most drugs have been defined by the World Health Organization.[6] Inpatient usage is usually expressed per 100 occupied bed days (OBD) to take into account variation in workload; however, this does not take into account case mix. Use of this internationally accepted standard enables the use of antibacterial agents with different doses to be compared, aggregation of data to assess usage of different antibacterial classes, and comparisons between centres. For example, the European Surveillance of Antibiotic Consumption (ESAC) project group has explored the use of this approach to measure antibacterial usage in both primary and secondary care across five years and 31 countries.[7,8] In primary care, higher consuming countries were found to have higher levels of resistance.[7] The Antibiotic Resistance Prevention and Control (ARPAC) group has also used this approach in 140 European hospitals.[9]

Our objectives were to obtain DDD data from our trust for three consecutive years, to compare data year-on-year, to compare our results with those from other sites both in the UK and elsewhere, and to identify any methodological issues encountered.

Methods

Setting Hammersmith Hospitals NHS Trust (HHNT) is a large teaching trust situated in west London, with four hospital sites and about 1,000 beds. Specialties include infectious diseases, oncology, haematology, cardiothoracic surgery, neurology and neonatal medicine. There are no paediatric or HIV beds.

Data collection and analysis Drug usage data for all drugs in British National Formulary section 5.1 (antibacterials) were obtained from the pharmacy computer system (AScribe version 8.6) for the three previous financial years. We included data for packs issued to inpatients only, either as ward stock or dispensed to individual patients. Discharge and outpatient supplies were excluded to facilitate comparison with European hospitals where such prescriptions are not dispensed by hospital pharmacies. However, any pre-labelled discharge packs of antibacterials supplied as ward stock were included, as these may be started during the hospital stay as part of our one-stop dispensing scheme.[10]

To convert pack usage into DDDs, we adapted an Excel spreadsheet previously developed at South Manchester University Hospitals NHS Trust (available at www.allaboutpharmacy.co.uk). The spreadsheet facilitated the calculation of DDDs based on the number of packs of each antibacterial used, the number of dose units in each pack and DDD values allocated by WHO. We created one row of the spreadsheet for each pack size of each drug. Where there was no WHO DDD for a given drug, we developed our own based on local

Table 1: Defined Daily Doses (DDDs) for antibacterials across three financial years

	Financial year 2002/03		Financial year 2003/04		Financial year 2004/05	
	Inpatient DDD (% of all DDD)	Inpatient DDD/100 OBD	Inpatient DDD (% of all DDD)	Inpatient DDD/100 OBD	Inpatient DDD (% of all DDD)	Inpatient DDD/100 OBD
Oral DDDs	170,363 (58.5)	50.8	183,273 (59.3)	50.7	176,571 (60.9)	55.7
IV DDDs	121,121 (41.5)	36.1	125,828 (34.8)	34.8	113,600 (39.1)	35.8
Total	291,484 (100.0)	86.9	309,101 (100.0)	85.5	290,171 (100.0)	91.5

"IV" means intravenous and "OBD" means occupied bed days. Antibacterials are those listed in section 5.1 of the British National Formulary.

clinical practice. The WHO DDD for intravenous co-amoxiclav changed in 2005. We used the 2005 value for all three years. The spreadsheet was also set up to calculate subtotals for individual drugs, classes and routes of administration. Rectal metronidazole was included with the oral dosage forms; intrathecal and nebulised preparations and gentamicin bone cement were included with the IV doses. The number of OBD was determined for each financial year studied, and the number of IV, oral and total DDDs expressed per 100 OBD.

Results

Results are summarised in Table 1. Antibacterial consumption ranged from 85.5 to 91.5 DDDs per 100 OBD across the three years studied. There was a 2.4 per cent decrease between financial years 02/03 and 03/04, followed by a 4.1 per cent increase between 03/04 and 04/05. The proportion of oral DDDs changed significantly over the three-year period ($P < 0.0001$; chi square test).

The group of antibacterials with the highest consumption was penicillins (Table 2), followed by cephalosporins. There were some minor changes over the three years but, in general, usage was consistent. There was a slight decrease in usage of third generation cephalosporins (data not shown). Table 3 (p135) presents our data compared with those obtained in other studies. About two and a half days of a pharmacist's time were required to enter the data for each financial year, although we expect that this could be done by administrative staff in future.

Discussion

We found that it was possible to calculate inpatient DDDs in a UK hospital setting. The statistically significant increase in the percentage of DDDs that were given orally, is encouraging in view of our efforts to encourage IV to oral switch[18] and in line with findings elsewhere.[19] Comparisons of this type would be more difficult using expenditure or quantity of packs issued, because of differences in costs and pack sizes between the two formulations. Our usage of antibacterials was in line with other UK sites for which data were available, but higher than outside the UK.

Methodological issues We encountered a range of methodological issues when considering how to apply DDD methodology to a UK site.

First, we decided to use BNF classifications and to limit our data to section 5.1. This classification is familiar to most UK health care professionals and was the system used to classify drugs in our pharmacy computer system. However, DDD data published outside the UK are presented according to the Anatomical Therapeutic Chemical (ATC) classification[1,7,8,13,15] and limited to ATC code J01 (antibacterials for systemic use). Although there is considerable overlap between BNF 5.1 and ATC J01, drugs specifically used to treat tuberculosis and leprosy are listed in BNF 5.1 but not in ATC J01. These are capreomycin, isoniazid, ethambutol, cycloserine, pyrazinamide, dapsone and clofazimine. This potentially limits comparisons that can be made between studies using the two approaches, although usage of these drugs is comparatively low (accounting for 2.6 DDDs per 100 OBD in year 2003–04 for our trust, or 3 per cent of all DDDs). There are also many drugs in ATC J01 that are not listed in BNF 5.1. However these are all alternative drugs such as a wide range of cephalosporins not marketed within the UK, rather than different classes of drug.

Second, we identified some drugs and formulations for which there was no WHO DDD, such as intrathecal vancomycin and gentamicin. We wanted to obtain comprehensive data and therefore decided our own DDD in these cases, using 10mg for intrathecal vancomycin (two DDDs per vial) and 1mg for intrathecal gentamicin (5 DDDs per vial). We recognise that in these cases, the DDD is generally less than one dose unit; usage may be artificially inflated because a whole vial may be used even if only one DDD is administered.

Third, we identified problems with how to address discharge medicines and inpatient medicines dispensed for discharge. We had decided to exclude outpatient and discharge use of antibacterials in line with other studies. However, it was not always possible to

Table 2: Defined Daily Doses (DDDs) per 100 occupied bed days (OBD) according to BNF subsection

BNF subsection	Financial year 2002/03	Financial year 2003/04	Financial year 2004/05
Penicillins	28.5 (32.6)	29.8 (34.9)	33.4 (36.5)
Cephalosporins	14.8 (16.9)	13.5 (15.8)	15.1 (16.5)
Metronidazole	7.6 (8.7)	7.2 (8.4)	9.3 (10.2)
Macrolides	7.0 (8.0)	6.8 (7.9)	9.8 (10.8)
Quinolones	7.6 (8.7)	7.5 (8.8)	7.6 (8.3)
Other antibacterials	4.4 (5.0)	4.2 (5.0)	5.8 (6.3)
Trimethoprim and sulphonamides	4.8 (5.5)	3.4 (4.0)	3.6 (3.9)
Aminoglycosides	3.4 (3.9)	3.6 (4.2)	3.4 (3.7)
Antituberculosis drugs	3.9 (4.5)	4.1 (4.8)	1.8 (2.0)
Tetracyclines	4.6 (5.3)	4.4 (5.2)	1.1 (1.2)
Clindamycin	0.6 (0.7)	0.4 (0.5)	0.4 (0.4)
Nitrofurantoin	0.1 (0.1)	0.1 (0.1)	0.2 (0.2)
Antileprotic drugs	0.1 (0.1)	0.3 (0.4)	0.0 (0.0)
Total DDDs per 100 OBD	87.4 (100)	85.3 (100)	91.5 (100)

Figures in brackets are the percentage of DDDs per 100 OBD attributable to that group of antibacterials. Totals differ slightly from those in Table 1 because figures have been rounded.

separate inpatient and discharge use where antibacterials were dispensed for discharge but started as an inpatient. We therefore included discharge packs supplied as ward stock within our figures but excluded any dispensed for individual patients. Use of such discharge packs is increasing and we may need to establish their relative inpatient and outpatient usage in order to decide whether or not their usage should be included as inpatient DDDs. Anecdotally, we have also observed considerable variation within the UK in relation to whether or not discharge supplies are included as inpatient DDDs.

Fourth, some logistical problems arose in relation to the way in which pack sizes were expressed on our computer system. Packs that should not be split, such as bottles of antibacterial suspension and pre-labelled discharge packs, were set up on our computer system with a pack size of one. However, to calculate the number of DDDs supplied, it is essential to know how many dose units are in each pack. Where packs were currently stocked we were able to ascertain this information, but it was not always possible to determine this retrospectively for discontinued packs or pack sizes that had changed over the period studied.

Fifth, in line with most previous studies, we expressed DDDs per 100 OBD. However, others have suggested that it may be more meaningful to express DDDs by finished consultant episode (FCE)[11] or by patient day or admission.[20]

Finally, for logistical reasons, we analysed data for entire financial years rather than for each month. However, this means that we have insufficient information about variability in use over time to explore any differences statistically. Instead the results highlight areas for further investigation.

Other methodological issues have been identified when making comparisons between countries for both primary and secondary care.[8] Specific issues for secondary care include variability in whether usage in nursing homes, private hospitals, day care centres and hospital outpatients is included, and difficulties in obtaining data on OBD.

Comparison with other sites Our usage in DDDs per 100 OBD was in line with that at other UK sites. However, usage outside the UK appears to be considerably lower. It is not known why this is the case. Possible explanations include differences in case mix and length of stay as well as differences in patterns of antibacterial use. Compared with ARPAC data from 140 European hospitals,[9] our usage of macrolides and tetracyclines was comparatively higher and usage of non-penicillin beta lactam antibacterials comparatively lower.

Limitations As with all usage data, this method does not provide any information on length of course, which may be important in development of resistance. Similarly, it does not provide any information on the indications for which antibacterials are prescribed or the combinations used. Point prevalence studies[5] or audits of specific issues are required if information of this type is required. Finally, care should be taken in interpreting data, because the DDD does not necessarily reflect the recommended or prescribed daily dose. Doses for individual patients and patient groups will often differ from the DDD, particularly in paediatrics.

Conclusions

It is possible to obtain data on DDDs in the UK hospital setting, although a variety of methodological issues may need to be addressed. Analysis of DDDs is likely to be a useful approach that can be used to complement point prevalence studies and may be useful to explore relationships between usage and resistance patterns. The ratio of oral and IV DDDs may also be useful for monitoring the impact of IV to oral switch programmes.

There is currently variability between sites in how DDD data are measured. There is no standard UK approach and little sharing of data. A standardised approach is needed, so that data obtained from different trusts can be compared in a meaningful manner both within the UK and internationally. Particular

Table 3: Summary of studies presenting antibacterial Defined Daily Dose (DDD) data

Source	Country/ region	Study setting	Study period	Classification used	Inpatient DDDs/ 100 OBD
Data in present paper	UK	Hammersmith Hospitals NHS Trust	Apr 2002–Mar 2003	BNF 5.1	86.9
Data in present paper	UK	Hammersmith Hospitals NHS Trust	Apr 2003–Mar 2004	BNF5.1	85.5
Data in present paper	UK	Hammersmith Hospitals NHS Trust	Apr 2004–Mar 2005	BNF 5.1	91.5
Williams S 2005 (personal communication)	UK	South Manchester University NHS Trust	Apr 2002–Mar 2003	BNF 5.1	105.5
Williams S 2005 (personal communication)	UK	South Manchester University NHS Trust	Apr 2003–Mar 2004	BNF 5.1	121.3
Jamieson C 2005 (personal communication)	UK	City Hospital, Birmingham	Apr 2003–Mar 2004	ATC J01	87.5
Ansari F 2005 (personal communication)	UK	Tayside University NHS Trust	May 2002–Apr 2003	ATC J01	73.1
Reference 2	UK	Royal Infirmary, Aberdeen	year 2000	ATC J01	93.8
Reference 11	UK	12 English district general hospitals	year 2002	ATC J01, BNF 5.1	119.8
Reference 12	Sweden	Department of Internal Medicine, Huddinge University Hospital, Stockholm	year 2000	ATC J01	39–57
Reference 13	Denmark	55 public hospitals (excluding emergency and psychiatric wards)	1997-2001	ATC J01	38.0–44.8
Reference 14	Netherlands	54 hospitals	1991-1996	ATC J01	37.3–42.5
Reference 15	France	49 hospitals	year 1999	ATC J01	40.2
Reference 16	Germany	Departments of internal medicine at eight teaching hospitals	1998-2000	ATC J01	55.2
Reference 9	Europe	140 hospitals	year 2001	ATC J01	55.0
Reference 17	Australia	Eight metropolitan hospitals	year 2002	ATC J01	70.0

"OBD" means occupied bed days, "BNF 5.1" means British National Formulary, Chapter 5.1, "ATC J01" means Anatomical Therapeutic Chemical Classification code J01 (ie, antibacterials for systemic use) issues needing to be addressed include the dataset used (BNF 5.1 or ATC J01), whether or not discharge medicines and antibacterials dispensed as part of one-stop dispensing schemes should be included, developing DDD values for drugs for which there is no WHO standard and agreeing the denominator used.

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