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2	<r.cooke@aston.ac.uk>Development of a prescribing indicator for</r.cooke@aston.ac.uk>
3	objective quantification of antibiotic usage in secondary care.
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7	
8	Abstract
9	
10	Objectives
11	To compare the recognised Defined Daily Dose per 100 bedday measure (DDD/100
12	bedday) with the Defined Daily Dose per Finished Consultant Episode (DDD/FCE) in
13	a group of hospitals with a variety of medicines management strategies.
14	To compare antibiotic usage using the above indicators in hospitals with and without
15	electronic prescribing systems.
16	
17	Methods
18	Twelve hospitals were used in the study. Nine hospitals were selected and split into
19	three cohorts (three high-scoring, three medium-scoring and three low-scoring) by
20	their 2001 Medicines Management self-assessment scores (MMAS). An additional
21	cohort of three electronic prescribing hospitals was included for comparison. MMAS
22	were compared to Antibiotic Management Scores (AMS) developed from a
23	questionnaire relating specifically to control of antibiotics. FCEs and occupied
24	beddays were obtained from published statistics and statistical analysis of the
25	DDD/100 beddays and DDD/FCE were carried out using SPSS.

1	
2	Results
3	The DDD/100 beddays varied from 81.33 to 189.37 whilst the DDD/FCE varied from
4	2.88 to 7.43. The two indicators showed a high degree of correlation $r = 0.74$ .
5	MMAS were from 9 to 22 (possible range 0 to 23) and the AMS from 2 to 13
6	(possible range 0 to 22). The two scores showed a high degree of correlation $r = 0.74$ .
7	No correlation was established between either indicator and either score.
8	
9	Conclusions
10	The WHO indicator for medicines utilisation, DDD/100 beddays, exhibited the same
11	level of conformity as that exhibited from the use of the DDD/FCE indicating that the
12	DDD/FCE is a useful additional indicator for identifying hospitals which require
13	further study.
14	
15	The MMAS can be assumed to be an accurate guide to antibiotic medicines
16	management controls.
17	
18	No relationship has been found between a high degree of medicines management
19	control and the quantity of antibiotic prescribed.
20	
21	Keywords
22	Antibiotic usage, Defined Daily Dose, prescribing indicator, secondary care.
23	
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## 1 Introduction

It has been estimated<sup>1</sup> that twenty per cent of medicines expenditure in England occurs in secondary care. However, there is little aggregated data relating to the use of medicines in this sector. Pilot work,<sup>2</sup> found that during the period between January 1997 and December 1998, antibiotics accounted for nineteen per cent of the total expenditure on medicines in secondary care, which was the highest spend of all categories of medicinal product. Participants within the study also highlighted that there was a need for a suitable indicator to facilitate benchmarking between hospitals.

9

10 The emergence of 'evidence based practice' during the NHS policy reforms of the 11 1990s was part of the change to create a culture in which clinical governance drives 12 individual hospital practitioners to examine their practice and compare it with their 13 peers. Pharmaceutical care, 'the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life'<sup>3</sup> defines the 14 15 scope of pharmaceutical responsibility in the use of medicines. This was supplemented by the 'medicines management' concept,<sup>4</sup> which developed the theme 16 17 of systems to control medicines usage from procurement, managed entry onto a 18 hospital formulary through to prescribing review and use of clinical guidelines. In 19 order to optimise the use of medicines, it is vital that therapeutic categories of 20 medicines where there is high-volume and high-cost are reviewed. It has been 21 established that antibiotics are often both high-volume and high-cost. In addition, it has been demonstrated<sup>5</sup> that a large percentage of antibiotic use in hospitals is 22 23 inappropriate.

24

1 Clearly, there is a requirement for multi-centre clinical audit of antibiotic usage. 2 However, in order to benchmark the use of antibiotics across the full spectrum of 3 secondary care settings, a robust measure is needed which is independent of workload, in order that comparisons can be made. The UK Department of Health has 4 recently allocated funding for each English hospital to use for promoting 'prudent use 5 of antibiotics<sup>2</sup>,<sup>6</sup> This initiative will enable work to commence to improve targeted 6 7 clinical pharmacy initiatives related to antibiotic use and also to begin to address 8 collection of data from hospitals.

9

A large amount of therapeutic guidance<sup>7-12</sup> has been published, which focuses on 10 11 antibiotic resistance and the use of antibiotics in medicine. Issues examined include 12 the use of formularies within hospitals, the process by which antibiotics are prescribed 13 by junior doctors, sensitivity testing and the surveillance of resistant organisms. One report<sup>13</sup> concluded that there was a lack of data on antimicrobial use in hospitals and 14 15 that hospitals should install computerised systems for patient specific prescribing.

16

17 The European Society for Clinical Microbiology and Infectious Disease (ESCMID) 18 established a study group on antibiotic policies (ESGAP) which in turn created a 19 number of sub-groups to develop strategy related to the stewardship of antibiotics within European hospitals. This group produced a number of recommendations<sup>14</sup> 20 21 which include a commendation that 'measurement of antibiotic consumption should 22 be performed with regular benchmarking of figures and discussion between 23 prescribers, pharmacists and infection specialists'.

24

The purpose of any indicator of prescribing is to enable comparisons to be made over time. The comparison may be between individual prescribers, wards, specialties, hospitals or geographical groups of hospitals. Measures are not definitive but act as a focus for the commencement of review and should act as a stimulus for change.

5

6 The need for an international classification system for drugs has been recognised for many years.<sup>15</sup> The Anatomical Therapeutic Chemical System (ATC), was developed 7 by the Norwegian Medicinal Depot, in Oslo, by modification of an existing system 8 9 that had been used by pharmaceutical market researchers in Europe. In addition to a 10 robust classification system it was necessary to develop a unit of measurement. The 11 Defined Daily Dose (DDD) was developed, also by the Norwegian Medicinal Depot 12 as a unit of measurement for use in drug utilisation studies. The ATC/DDD system, 13 was recommended for international drug utilisation studies by the World Health 14 Organisation (WHO) in 1981. The purpose of the ATC/DDD system is to act as a tool 15 for drug utilisation research so that the quality of drug usage will improve.

16

The DDD is defined<sup>16</sup> as 'the assumed average maintenance dose per day for a drug 17 18 used for its main indication in adults'. A DDD is only assigned when a compound has 19 been given an ATC code. All of the ATC codes and DDD data are published in the ATC Index.<sup>17</sup> The DDD is not a reflection of a prescribed or recommended daily 20 21 dose. It represents a unit of measurement to enable researchers to identify trends in 22 consumption of medicines and to compare the exposure to specific medicines of 23 population groups. The DDD is a compromise in that it is based on a review of doses 24 used in a variety of countries. The DDD will normally be associated with a

- denominator to correct for workload variations. For hospital in-patients the number of
   DDDs per 100 beddays is normally used.
- 3

A study of the DDD system<sup>18</sup> compared the approach of Europeans to undertaking
drug utilisation review with that of the North Americans which has focussed more on
review of individual prescribers and individual drug regimens in order to optimise
patient treatments.

8

9 This study concluded that the DDD system would serve as a valuable additional tool 10 for drug utilisation studies. A further study carried out to evaluate DDD 11 methodology<sup>19</sup> concluded that calculation of the DDD was a valuable first step in 12 measuring total drug use in a population, but that for more precise estimates of drug 13 use, other techniques would also be required.

14

An antibiotic usage measure developed in 1998 within our group<sup>20</sup> has been applied previously to the usage of quinolone antibiotics. In order to more fully evaluate the usefulness of this measure as a tool to compare antibiotic utilisation, the present study compares the recognised DDD/100 bedday measure with the DDD/FCE in a group of hospitals with a variety of medicines management strategies.

20

## 21 Materials and method

Four cohorts of three hospitals were used as data collection sites. These hospitals were selected for their differing inter-group characteristics, in terms of size, workload, case-mix and medicines management strategy. The sample size was 6.65% of hospital activity in England based on the total number of FCEs completed in the year 2001/2

1	(822,445 FCEs from a total of 12,357,360; data obtained from Hospital Episode
2	Statistics 2001/2 Department of Health, London). A Finished Consultant Episode
3	(FCE) being defined as 'a period of healthcare under one Consultant, in one hospital
4	provider <sup>2</sup> . <sup>21</sup>
5	
6	Antibiotic usage data was collected for systemic antibacterials (ATC category J01).
7	
8	The number of occupied beddays and FCEs for each Trust for 2001/2 was recorded
9	from the Department of Health published Hospital Episode Statistics.
10	
11	The hospitals were selected on the basis of their medicines management self-
12	assessment scores arising from a nationally sponsored self-assessment exercise carried
13	out at the beginning of 2001. <sup>22</sup> This self-assessment consisted of six equally weighted
14	domains of activity related to medicines management, with a high score being
15	indicative of a high degree of control of medicines usage. The maximum possible
16	aggregate score was 23. The six-domains were as follows –
17	• Senior management awareness and involvement
18	• Information and financial issues
19	• Medicines policy management, including the introduction of new drugs
20	Procurement of medicines
21	• The primary and secondary care interface
22	• Influencing prescribers
23	
24	It was felt that the scores from this exercise would be indicative of the degree of

25 control and influence over the general use of medicines and more specifically,

antibiotics, and that high scores in this measure would be linked to low levels of
antibiotic usage (divergent validity).
Reviewing the scores for hospitals in the West Midlands, it was possible to select
three high-scoring hospitals (score >19), together with three medium scoring hospitals
(score >15 but < 19) and a third group with lower scores (score <15).</li>

7

8 In addition, to these nine hospitals it was felt that the three English hospitals that have 9 fully implemented electronic prescribing systems would be used as a discrete 10 comparator reflecting the potential importance of electronic prescribing systems in 11 controlling medicines usage. The characteristics of the hospital trusts participating in 12 the present study are summarised in Table 1.

13

14 In order to validate the medicines management scores which relate to general control 15 systems in place for all medicines, a questionnaire was designed containing questions 16 covering 11 aspects of medicines management relating specifically to control of the 17 use of antibiotics. This ensured consistency in interpretation of the questions across 18 the sample. The data generated from the questionnaire would also support and cross-19 reference the results from the medicines management self-assessment tool. The 20 questions covered areas of recognised good practice in control of antibiotic usage and 21 included – audit of usage, data sharing between pharmacy and microbiology departments, liaison with Infection Control services, pharmacy led educational 22 23 initiatives, pharmacist empowerment to convert from IV to oral routes, pharmacist 24 discontinuation of therapy and rationalisation of formulary choices of antibiotics.

25 The maximum possible score for this assessment was 22.

- 1 Statistical treatments
- 2 Data was entered into a flatfield database and analysed using the SPSS version 11
  3 software package.
- 4

5 <b>Results</b>	

Table 2 lists each Trust included in the present study with details of activity, the total
number of DDDs of antibiotic used in 2001/2 and the derived prescribing indicators
and Medicines Management scores.

- 9
- 10 The range of Medicines Management scores was from 9 to 22 and the Antibiotic

11 Management Scores ranged from 2 to 13. The DDD/100 beddays varied from 81.33 to

12 189.37 (mean 114.62). The DDD/FCE varied from 2.88 to 7.43 (mean 4.1).

- 14 Figure 1 shows the correlation of the two prescribing indicators (Pearson correlation r
- 15 = 0.74). Figure 2 shows the correlation of the medicines management scores (Pearson
- 16 correlation r = 0.74).
- 17

## 1 Discussion

2 The present study has evaluated the performance of two prescribing indicators, one 3 established, the other experimental, in assessing antibiotic prescribing in a range of UK hospital trusts. The DDD/FCE and DDD/100 bedday results did show a 4 significant correlation (r = 0.74). It was felt that this demonstrated the robustness of 5 the proposed indicator as an additional measure for use when antibiotic drug 6 utilisation studies are being carried out. This in turn facilitates the identification of 7 8 hospitals where more detailed or specialised analysis of antibiotic prescribing is 9 required. 10 11 The electronic prescribing group had the lowest mean usage 3.5 DDD/FCE. It is likely 12 that the use of a computerised prescribing system enhances good practice in 13 prescribing by allowing pre-agreed 'stop dates' to be programmed together with 14 reminders about reviewing treatment and by providing a greater degree of formulary control. It would be valuable for a prospective study to be carried out to establish 15 16 whether this is the case. 17 18 The total antibiotic usage figures for the twelve hospitals varied from 81.33 - 189.3719 DDD/100 beddays (mean 114.6). These findings can be compared with data from various European studies which found usage at 37.2 - 42.5,  $^{23}$  41 - 51<sup>24</sup> and 25-68.  $^{25}$ 20 21 It may be that the much higher rates of antibiotic usage found in this study reflect a

22 difference in the categories of patients that are included in secondary care activity data

- and how the English health care system operates.
- 24

1	The results do not show an association between a high score in either of the medicines
2	management scores and a low value for the two prescribing indicators of antibiotic
3	usage (Table 2). This lack of relationship leads to a conclusion that enhancing
4	medicines management controls may not reduce antibiotic prescribing. These findings
5	may indicate that antibiotic prescribing patterns within the study hospitals are subject
6	to influences not embraced by the indicators employed. Such factors may include the
7	morbidity of the hospital's catchment population, the casemix of patients treated,
8	which in turn will be governed by the service profile offered by each hospital in terms
9	of specialties and number of beds devoted to each specialty.
10	
11	A morbidity profile for the catchment population of an individual hospital can be
12	created from analysis of the Primary Care Trust of residence of patients treated and
13	linking this to morbidity measures obtained from census data. This work is on-going.
14	The influence of casemix will influence the WHO measure (DDD/100 beddays) to a
15	greater degree than the DDD/FCE, since variations in casemix e.g. more surgical
16	beds, would decrease the average length of stay within a hospital, whilst conversely a
17	greater proportion of Care of the Elderly beds will generally increase the average
18	length of stay.
19	

than bedday numbers, as it is a measure of episodes of individual care. However, in
some cases the episode of care may involve a number of Consultants that can lead to
it being counted as more than one FCE.

The FCE is more closely linked to individual in-patient exposure rates to antibiotics

24

1 It is apparent that additional data is needed before conclusions about the quality of 2 antibiotic usage in a specific hospital can be drawn. The specific profile of antibiotic use by therapeutic group for each hospital, together with local bacterial resistance 3 4 data, would provide valuable comparative data. This will need to be linked to morbidity data and the usage data linked to activity will require monitoring over a 5 6 number of years in order to determine the effects of controls systems, be they 7 electronic prescribing systems, utilisation of pharmacists with a remit to change antibiotic prescribing habits or the establishment of multidisciplinary review teams. In 8 9 order to maximise the opportunity for change to occur pharmacists will need to work 10 closely with microbiologists to influence prescribing habits. 11 12 The Medicines Management self-assessment score (MMAS) and the Antibiotic 13 Medicines Management score (AMS) showed a high degree of correlation (r = 0.74), which demonstrates that the MMAS is a valid indicator of antibiotic medicines 14 management arrangements. 15

## 1 Conclusion

- 2 The WHO indicator for medicines utilisation, DDD/100 beddays, showed the same
- 3 level of conformity which was exhibited from the use of the DDD/FCE (r = 0.74)
- 4 indicating that the DDD/FCE is a useful indicator for identifying hospitals which
- 5 require further study.
- 6 The present study has highlighted the following points:
- 7
- 8 It is proposed that both the DDD/100beddays and the DDD/FCE are used to
  9 compare antibiotic usage between hospitals in England.
- The electronic prescribing cohort showed the lowest level of usage
   (DDD/FCE) which may indicate the value of computerised prescribing
   systems in promoting appropriate antibiotic prescribing.
- Medicines Management measures are only a single contributor to a hospitals
   antibiotic usage profile and may influence quality but not quantity of
   antibiotic prescribed.
- Further work over a number of years is required to establish trends to validate
  these results.
- 18
- 19

## **References**

2	1.	Consumers' Association. (1997). Medicines and the NHS: a guide for						
3		directors. Consumers' Association, London, UK.						
4	2.	National Prescribing Centre. (1999). Hospital Prescribing Information Project,						
5		Second report. Analysis for Health Authority Prescribing Advisers and Senior						
6		Hospital Professionals/Managers. National Prescribing Centre, Liverpool, UK.						
7	3.	Hepler, D. & Strand, L. (1990) Opportunities and responsibilities in						
8		pharmaceutical care. American Journal of Hospital Pharmacy 47, 533-543.						
9	4.	Fitzpatrick, R., Mucklow, J. C. & Fillingham, D. (2001). A comprehensive						
10		system for managing medicines in secondary care. Pharmaceutical Journal						
11		<b>266,</b> 585-588.						
12	5.	Castle, M., Wilfert, C. M., Cate, T. R. et al. (1977). Antibiotic use at Duke						
13		University Medical Centre. Journal of the American Medical Association 237,						
		0010 0000						
14		2819-2822.						
14 15	6.	Department of Health (2003). Hospital Pharmacy initiative for promoting						
	6.							
15	6.	Department of Health (2003). Hospital Pharmacy initiative for promoting						
15 16		Department of Health (2003). Hospital Pharmacy initiative for promoting prudent use of antibiotics in hospitals. Department of Health, London, UK.						
15 16 17		Department of Health (2003). Hospital Pharmacy initiative for promoting prudent use of antibiotics in hospitals. Department of Health, London, UK. (PL/PhO/2003/3).						
15 16 17 18	7.	Department of Health (2003). Hospital Pharmacy initiative for promoting prudent use of antibiotics in hospitals. Department of Health, London, UK. (PL/PhO/2003/3). World Health Organization. (2001). WHO Global Strategy for Containment of						
15 16 17 18 19	7.	Department of Health (2003). Hospital Pharmacy initiative for promoting prudent use of antibiotics in hospitals. Department of Health, London, UK. (PL/PhO/2003/3). World Health Organization. (2001). WHO Global Strategy for Containment of Antimicrobial Resistance. World Health Organization, Geneva.						
15 16 17 18 19 20	7. 8.	Department of Health (2003). Hospital Pharmacy initiative for promoting prudent use of antibiotics in hospitals. Department of Health, London, UK. (PL/PhO/2003/3). World Health Organization. (2001). WHO Global Strategy for Containment of Antimicrobial Resistance. World Health Organization, Geneva. U.S. Congress. (1995). Impacts of Antibiotic-Resistant Bacteria. Office of						
15 16 17 18 19 20 21	7. 8.	Department of Health (2003). Hospital Pharmacy initiative for promoting prudent use of antibiotics in hospitals. Department of Health, London, UK. (PL/PhO/2003/3). World Health Organization. (2001). WHO Global Strategy for Containment of Antimicrobial Resistance. World Health Organization, Geneva. U.S. Congress. (1995). Impacts of Antibiotic-Resistant Bacteria. Office of Technology Assessment, Washington DC, USA.						

1	10. Department of Health. (1999). Resistance to Antibiotics and other
2	Antimicrobial agents. Department of Health, London, UK. (HSC1999/049).
3	11. Department of Health. (2000). UK Antimicrobial Resistance Strategy and
4	Action Plan, pp. 1-23. Department of Health, London, UK.
5	12. Department of Health. (1998). The path of least resistance. Main report of the
6	Standing Medical Advisory Committee, sub-group on antimicrobial resistance,
7	pp. 152. Department of Health, London, UK.
8	13. Select Committee on Science and Technology. (1998). Resistance to
9	antibiotics and other antimicrobial agents. House of Lords, Select Committee
10	on Science and Technology, London, UK.
11	14. Gould, I. M. (2001). Minimum antibiotic stewardship measures. Clinical
12	Microbiology and Infection 7, Suppl. 6, 22-26.
13	15. Capella, D. (1993). Descriptive tools and analysis. In Drug utilisation studies.
14	Methods and uses, (Dukes, M. N. G., Ed), pp. 55-78. WHO Regional
15	Publications, WHO Regional Office for Europe, Copenhagen.
16	16. United Kingdom Drug Utilisation Research Group. (2000). Handbook of Drug
17	Use Research Methodology, 1st edn, (McGavock, H., ed), pp 255. Prescription
18	Pricing Authority, Newcastle upon Tyne, UK.
19	17. WHO Collaborating Centre for Drug Statistics Methodology. (1999). ATC
20	Index with DDDs. Oslo, Norway.
21	18. Wertheimer, A. I. (1986). The defined daily dose (DDD) system for drug
22	utilization review. Hospital Pharmacy 21, 233-258.
23	19. Wessling, A. & G. Boethius. (1990). Measurement of drug use in a defined
24	population. Evaluation of the defined daily dose (DDD) methodology.
25	European Journal of Clinical Pharmacology <b>39</b> , 207-210.

1	20. Curtis, C. E., Fitzpatrick, R. & Marriott, J.F. (2002) An evaluation of
2	quinolone prescribing in a group of acute hospitals: development of an
3	objective measure of usage. Pharmacy World and Science 24, 161-166.
4	21. Department of Health 2004. HES Factsheet, Glossary of Terms. Department of
5	Health, London, UK.
6	22. Department of Health press release 12 December 2000. Health Minister Lord
7	Hunt announces new framework to assess medicines management systems in
8	hospitals. Department of Health, London, UK. (2000/0733).
9	23. Janknegt, R., Oude Lashof, A., Gould, I. M. et al. (2000). Antibiotic use in
10	Dutch hospitals 1991-1996. Journal of Antimicrobial Chemotherapy 45, 251-
11	256.
12	24. Kiivet, R. A., Dahl, M. L., Llerena, A. et al. (1998). Antibiotic use in 3
13	European university hospitals. Scandinavian Journal of Infectious Diseases 30,
14	277-280.
15	25. Vlahovic-Palcevski, V., Morovic, M., Palcevski, G., Betica-Radic, L. (2001).
16	Antimicrobial utilization and bacterial resistance at three different hospitals.
17	<i>Eur J Epidemiol</i> <b>17</b> (4), 375-383.
18	

Hospital	Comment	Number of beds	Cohort
1	Urban acute trust	1347	А
2	Urban acute trust	1330	А
3	Urban acute trust	811	А
4	Small town, electronic prescribing	465	В
5	Suburban, electronic prescribing	1279	В
6	County town, electronic prescribing	569	В
7	Urban acute trust	956	С
8	Urban trust	634	С
9	Urban trust (with infectious disease unit)	1320	С
10	Suburban trust	503	D
11	Specialist trust	227	D
12	County town	630	D

Table 1. Hospital sites included in the present study

Cohort A Medicines Management self assessment score (MMAS) >19

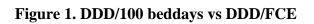
Cohort B Electronic prescribing site

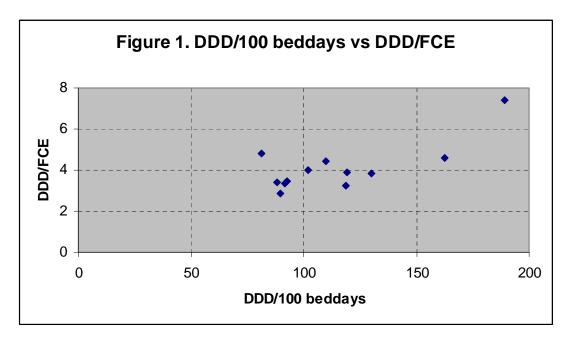
Cohort C Medicines Management self assessment score (MMAS) >15 & <19

Cohort D Medicines management self assessment score (MMAS) <15

Hospital (cohort)	FCEs	Beddays	DDDs	DDD/ 100beddays	DDD/ FCE	Medicines Management score (max 23)	Antibiotic management score (max 22)
1 (A)	93626	376259	413011	109.76	4.41	20	6
2 (A)	124357	339618	403806	118.9	3.24	20	11
3 (A)	72193	203178	330315	162.57	4.57	19.5	11
4 (B)	48047	142560	185511	130.1	3.86	16	11
5 (B)	97215	373071	328851	88.14	3.38	22	13
6 (B)	45225	166047	152055	91.57	3.35	16	4
7 (C)	66845	263099	268607	102.09	4.01	17.5	8
8 (C)	49856	186924	173368	92.74	3.47	17	6
9 (C)	103607	406430	769661	189.37	7.43	16	3
10 (D)	54963	176542	158421	89.73	2.88	14	7
11 (D)	8984	52906	43032	81.33	4.79	9	2
12 (D)	53192	173265	206543	119.2	3.88	13	3

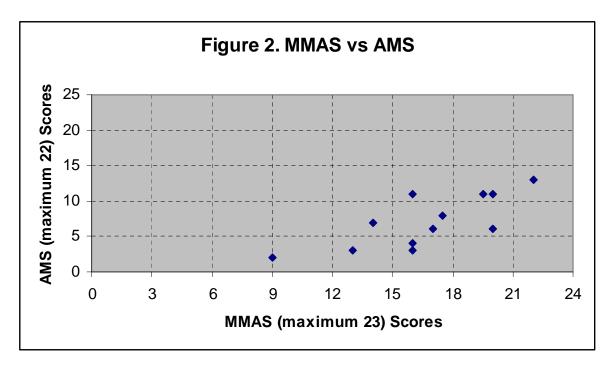
# Table 2. Summary data 2001/2





**Pearson correlation r = 0.74.** 





Pearson correlation r = 0.74.