Hospital Pharmacists

and their role in

adverse drug reaction reporting.

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Abstract

The problems associated with adverse drug reactions are well known. This thesis describes an assessment of the detection and reporting of adverse drug reactions (ADRs) by hospital pharmacists and by hospital pharmacy departments. Methods of increasing ADR reporting rates and, methods of improving the documentation and communication of data relating to ADRs are also investigated.

Relatively few hospitals in the UK have local ADR reporting schemes and where they exist, they are pharmacy-led. The number of reports received by schemes tends to be low and previous estimates of under-reporting appear to be over-optimistic. Systems for ensuring the appropriate documentation and communication of ADRs and for monitoring the effects of newly marketed drugs were rare. A large increase in one local ADR scheme's reporting rates was achieved using passive promotional methods. General practitioners consider that the communication of ADR data from secondary to primary care is of a poor quality. The introduction of an notification and reporting system, HAROLD, described in this thesis was viewed positively. ADR-related admissions were identified as a significant problem and many of the ADRs concerned are similar to those that have been reported for a number of years.

Using qualitative and quantitative analysis, this research found that hospital pharmacists viewed ADR reporting positively. Pharmacists have a reasonable knowledge of the Yellow Card Scheme and consider it a professional obligation to participate in it. Time appears to be a deterrent to reporting and despite having a good knowledge of the operation and purpose of the Yellow Card Scheme, pharmacists appear to be selective about which reactions they are prepared to report. Education and training were identified as key initiatives which could increase reporting rates.

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List of abbreviations

ABPI - Association of British Pharmaceutical Industry

ADR - Adverse Drug Reaction

ADRAC - Adverse Drug Reactions Advisory Committee

BTD - Black triangle drug

CDARRP - Canadian Drug Adverse Reaction Reporting Program

CSM - Committee on Safety of Medicines

MCA - Medicines Control Agency

NHS - National Health Service

PEM – Prescription Event Monitoring

RLUH - Royal Liverpool University Hospital

RMC - Regional Monitoring Centre (of the CSM)

List of publications and presentations associated with this thesis.

Research Papers.

1. Green CF, Mottram DR, Rowe PH, Brown AM. An investigation into adverse drug reaction monitoring by United Kingdom hospital pharmacy departments. International Journal of Pharmacy Practice. 1997; 5: 202-8.
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8. Green CF, Mottram DR, Rowe PH, Brown AM, Pirmohamed M. Adverse drug reaction reporting and hospital pharmacists: a postal questionnaire. United Kingdom Clinical Pharmacy Association. Proceedings of the Autumn Symposium. 1999; 11-12.

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Chapter 1:

Introduction

Chapter 1: Introduction

1.1 Adverse Drug Reactions (ADRs) - a definition.

A response to a drug which is noxious and unintended and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for the modification of a physiological function.

World Health Organisation, 1970[1]

The World Health Organisation definition of an ADR is used in this thesis as it is specific to the purposes of this research. The definition excludes events such as errors in drug administration and instances of intentional or unintentional poisoning or overdose which other definitions may include. This definition is widely used in literature describing the study of ADRs and is adhered to throughout this thesis.

1.2 ADRs: the size of the problem.

Estimated incidences of ADRs vary for a number of reasons. The population in question will affect the incidence of reported ADRs; for example, young patients requiring minor surgery and taking few medicines are less likely to suffer an ADR than an elderly patient suffering several clinical conditions receiving polypharmacy.[2,3] Variation in the precise definition of an ADR, differences in sample sizes investigated, that many ADRs are unreported or unidentified and the influence of specific specialities (for example, an excess of surgical or renal patients) may greatly affect the estimated incidence of ADRs.

A review of studies examining ADR-related admissions to hospitals found that reported rates varied from 0.2% to 21.7% with an average rate of 5.5%.[4] Recent work has suggested that 6.7% of hospital patients suffer 'serious' ADRs while 0.32% of hospital patients suffer fatal ADRs. Indeed ADRs have been suggested to have been between the fourth and sixth leading cause of death in the USA in 1994.[5]

1.3 Why ADRs are a problem.

ADRs are a problem because they may:

- complicate existing disease
- cause hospital admissions
- affect quality of life
- delay relief or cure of the disease which they were intended to treat
- mimic other disease states
- result in inappropriate treatment of unrecognised, drug-induced problems
- cause a patient to lose confidence in their carers and their medicines resulting in poor compliance and consequently, treatment failure.[6]

1.4 Clinical Trials.

Clinical trials have numerous purposes and aim to demonstrate a drug's effectiveness and safety; however, they have a number of limitations. The numbers of patients involved in clinical trials are often limited due to the complexity of the investigations, monitoring of patients, co-ordination of trials and ultimately, cost. Patients are selected for clinical trials using specific criteria and it is unlikely that many different concurrent pathologies and drug therapies

will be encountered. Thus, the detection of certain drug-disease and drug-drug interactions and identification of long term side effects of drug therapy may not become apparent for a number of years after marketing and exposure to a larger unbiased population. Trials may also fail to obtain substantial data about the use of the agent concerned in very young or very old patients. Once marketed, drugs are often used for purposes other than those for which they were licensed, the so called "off-label" use, which may disclose further problems with a drug's safety profile. Due to the limits placed on the numbers of patients involved, clinical trials are also ineffective at detecting very rare ADRs. As few as 1000 patients may have been exposed to a new therapeutic agent or device prior to its marketing and it is thought that ADRs with an incidence of less than 1 in 250 are unlikely to be detected.[7] In order to verify that drugs are as safe as clinical trials have suggested, it is therefore vital that post marketing surveillance is carried out to monitor the safety of these agents.

1.5 Aims of post marketing surveillance.

The aims of post marketing surveillance are the detection of previously unrecognised ADRs, to identify risk factors for ADRs in individual patients, to collate data concerning recognised ADRs and ultimately to determine the safety of drugs. It may be used to encourage the safe and effective use of drugs that have been licensed. 'Signals', generated by reports of ADRs, spontaneous or otherwise, provide suggestions of associations between drugs and potential hazards. These may then be followed up by more formal methods of pharmacovigilance, particularly if the 'signal' is strong, if it is new, if it is deemed clinically important and if preventative measures are possible.

1.6 Origins of pharmacovigilance in the United Kingdom.

Although descriptions of adverse drug reactions have been reported for two thousand years, the first ADRs applying to "modern" medicine were observed in 1848 when a 15-year-old child died as a result of chloroform anaesthetic.[8] As a result of concerns about the safety of anaesthetics, a commission was established to collate reports of anaesthetic related deaths, the findings of which were published in 'The Lancet' in 1893.[9] Almost a half a century later, the deaths of 107 patients exposed to diethylene glycol used as a solvent for sulphanilamide resulted in legislative developments in the USA in 1938.[10] However, it was another 23 years until pharmacovigilance was to be seriously explored.

Thalidomide was first marketed in 1956 in Germany as 'Distival' and promoted as a treatment for insomnia and nausea in pregnancy. Reports of foetal abnormalities, phocomelia and micromelia, thought to have been caused by thalidomide were first published in the medical literature in 1961[11] and it is now estimated that over 8000 babies were born with thalidomide-related deformities.[12] Almost 40 years after this tragedy, thalidomide remains a household name, synonymous with adverse and undesirable effects of drugs.

As a result of the thalidomide tragedy and other less publicised but not dissimilar incidents, many countries decided that drug safety should become a priority. Prior to this, drugs could be marketed with little regard to their safety and efficacy. In the United Kingdom, with the co-operation of the Association of British Pharmaceutical Industry (ABPI) and the Proprietary Association, the Committee on Safety of Drugs (CSD) was established in 1963, becoming

operational on January 1st, 1964. Under the Chairmanship of Sir Derek Dunlop, the Committee's function was to monitor drug safety throughout the UK, to monitor and approve the introduction of new drugs, and to collect and act upon reports of adverse drug reactions.

In 1968, the Medicines Act brought into effect several new laws relating to the marketing of therapeutic and diagnostic agents. In September 1971, under Section 4 of the Medicines Act, the Committee on Safety of Medicines (CSM) replaced the Committee on Safety of Drugs. Although the membership of the committee did not greatly alter, the new committee now had statutory backing and authority.

1.7 The Medicines Control Agency.

The Medicines Control Agency (MCA) is the licensing arm of the UK's Drug Licensing Authority and is responsible for all aspects of the regulation of medicines in the UK. This includes the regulation of clinical trials, licensing medicines and monitoring their safety once on the market, investigating possible hazards and taking appropriate action to minimise the risks to users, protecting public health, inspection of premises manufacturing medicines and taking enforcement action if activities fall outside legal guidelines.[13]

1.8 The Committee on Safety of Medicines and Regional Monitoring Centres.

The CSM is a sub-division of the MCA and provides expert advice to the UK's Drug Licensing Authority on questions of safety, quality and efficacy of

medicines. It is also responsible for encouraging the collection and investigation of reports on suspected adverse reactions to medicines already on the market.

The CSM and MCA jointly run the Yellow Card Scheme. Using the Yellow Cards provided, reports are sent directly to the CSM / MCA or to one of the Regional Monitoring Centres (RMCs). These RMCs are associated with regional drug information services and local university departments of clinical pharmacology and pharmacists played an important role in their inception. Their aim is to stimulate ADR reporting by improving communications and providing feedback and follow-up to local reporters. Some RMCs publish regular newsletters concerning locally reported ADRs in an attempt to generate interest in pharmacovigilance.

1.9 The Yellow Card Scheme.

In 1964, the Committee on Safety of Drugs provided doctors and dentists with pre-paid yellow postcards with which to report adverse reactions to drugs thus creating the Yellow Card Scheme. Remodelled Yellow Cards may now be found in NHS prescription pads, the British National Formulary (BNF), The Compendium of Data Sheets and Summaries of Product Characteristics (formerly the ABPI Data Sheet Compendium), Monthly Index of Medical Specialities (MIMS) or may be obtained from the CSM / MCA. Nurses are not allowed to participate in the Yellow Card Scheme at present although a pilot scheme evaluating their potential role has recently been conducted.[14]

Over 350 000 Yellow Card ADR reports have now been made to the CSM / MCA and stored in their database. This database, the Adverse Drug Reactions On-line Tracking (ADROIT) system, is used to monitor Yellow Card reports, detect trends in reporting and improve the speed at which problems may be detected.[15] Yellow Card reports are made to the CSM / MCA in confidence and personal details of reporters and patients are neither published nor used for purposes of litigation. Data collected by the Yellow Card Scheme are not only used for national drug safety surveillance but also for international surveillance. Along with several other countries, the United Kingdom submits reports of ADRs to the World Health Organisation's Adverse Drug Reaction Collaborating Centre where data are collated for international use.

1.10 Action taken by the CSM / MCA.

Once a specific problem has been identified with regard to a certain product, the CSM / MCA may take action in a number of ways. The CSM / MCA may choose to advise individual doctors as to the adverse effects of certain drugs. They may also publish their findings and advice to prescribers in 'Current Problems in Pharmacovigilance', a communication used to disseminate information about ADRs to doctors and pharmacists. Analysis of ADR reports received by the CSM / MCA may also result in the withdrawal of drugs from the market or the amendment of product licences. For example, terfenadine has recently had its classification amended from a 'Pharmacy' medicine to a 'prescription only medicine' (POM).[16] The CSM / MCA may also publish warnings in the British National Formulary to highlight particular aspects of drug safety.[17] Examples of this include warnings about the use of beta-blockers in asthmatics, the risks of

developing agranulocyctosis with carbimazole and the need to monitor hepatic function with cyproterone acetate.

1.11 Under reporting of ADRs.

Under reporting of ADRs is considered to be a long standing problem with several reasons thought to contribute to its persistence. It has been suggested that the incidence of reporting of serious ADRs is, at best, in the order of 10% and for non-serious ADRs it is estimated at 2-4%.[18] The data obtained through the Yellow Card Scheme is therefore incomplete and indeed, it is likely that many serious and fatal reactions are never brought to the attention of the regulatory authorities. Factors considered to dissuade potential reporters (medical practitioners) from completing an ADR report, are shown in Box 1.1.[19,20,21] The concept of a fee has been proposed as a method of stimulating reporting and research has shown that a fee-based incentive can increase reporting rates but that on withdrawal of the fee, reporting rates fell substantially.[22]

Box 1.1: Factors affecting reporting of ADRs

Reaction not severe enough

Reaction well known

Familiarity with the suspect drug concerned

Concern over potential legal implications

Reaction may be predictable or expected

Ignorance of how to report an ADR

Lack of time, lethargy or complacency

Lack of feedback following previous reports

Failure to identify the presence of an ADR

Guilt because of patient suffering

Lack of confidence in making a report

The data collected in the Yellow Card Scheme are also open to significant bias and caution should be exercised in their interpretation. Reports of reactions appearing in the medical or lay press may result in numerous similar reports being submitted to the CSM / MCA. In turn, this may result in a 'false positive' or 'true positive' sign that a problem exists. An example of a 'false positive' is the association of suicidal ideation with fluoxetine (Prozac), a concept perpetuated by the media and refuted by the authorities in pharmacovigilance.[18] An example of a 'true positive' is the association of paroxetine (Seroxat) with acute withdrawal symptoms in patients stopping therapy, which was found on further analysis to be substantiated.[18]

The lessons of the practolol-induced oculomucocutaneous syndrome are worth noting. Following publication of a report on this syndrome in the medical press, over 200 reports of a similar nature were subsequently submitted to the CSM / MCA. Prior to the publication of the first report, only one report had been made to the CSM / MCA in four years.[19] This suggests that either practitioners had failed to associate a serious syndrome with a patient's drug therapy or that they had, but were unwilling to report it either because it was unrecognised or for other reasons.

1.12 Successes of the Yellow Card Scheme.

The CSM / MCA has been responsible for the identification of a number of important ADRs. Examples of successes of the scheme are outlined in Table 1.1.[18] The Yellow Card Scheme has provided important information concerning factors which may predispose patients to ADRs such as age, concurrent disease and concurrent medication; for example, the CSM / MCA suggests a reduced dose of azapropazone for the over 60s.[23] The Yellow Card Scheme has also allowed comparison between drugs in the same class; for example, the comparison between different NSAIDs to identify those with the greater risk of different adverse effects.[24] However, as discussed earlier, under reporting and biased reporting can distort true comparisons between different drugs.

Table 1.1: Notable successes of the Yellow Card Scheme since 1993.[18]

Drug (*Trade name*)	ADR reported	*Action taken*
Clozapine (*Clozaril*)	Myocarditis	*Additional warnings in product data sheet*
Remoxipride (*Roxiam*)	Aplastic anaemia	*World-wide withdrawal by manufacturers*
Rifabutin (*Myobutin*)	Uveitis / drug interactions	*Additional warnings and dose reduction*
Tiaprofenic acid (*Surgam*)	Severe cystitis	*Additional warnings augmented and contra-indications altered*
Cyproterone acetate (*Cyprostat, Androcur*)	Hepatotoxicity	*Indications restricted and requirement for hepatic monitoring introduced*
Alendronate (*Fosamax*)	Severe oesophageal reactions	*Additional warnings and altered dosing instructions*
Tacrolimus (*Prograf*)	Hypertrophic cardiomyopathy	*Additional warnings, dose reduction and monitoring required.*
Tramadol (*Zydol*)	Psychiatric reactions	*Additional warnings*

1.13 Intensive monitoring of newly marketed agents.

Inverted black triangles▼ are assigned to drugs new to the UK market or when drugs become available within new combinations of drugs, by a new, significantly different route of administration, or, as a novel drug delivery system. Drugs are initially assigned the black triangle symbol for a minimum of two years and the CSM request all reactions be reported for these drugs, regardless of their estimated causality or seriousness. However, in instances where there are particular concerns over the safety of a drug, it may retain the black triangle symbol for a longer period, for example tramadol (association with psychiatric disorders) and lamotrigine (association with serious skin disorders). Black triangle drugs are identified in the British National Formulary, Monthly Index of Medical Specialities, Summary of Product Characteristics & Data Sheet Compendium and all promotional material. A current list of black triangle drugs is maintained and made available, on request, by the CSM / MCA.

The limitations of clinical trials have been discussed earlier (section 1.4). Thus, the detection of rare ADRs, be it due to underlying pathology, drug-drug interactions, drug-disease interactions, delayed onset or to their bizarre or unexpected nature, may not occur until long after the drug has been marketed. Reporting of ADRs to newly marketed drugs, that is, those marked with a black triangle▼ is particularly important.

1.14 Monitoring of established drugs

Once drugs are no longer under intensive surveillance, the black triangle is removed and the emphasis on ADR surveillance alters. Relatively minor or well

documented reactions become less significant and instead of reporting all reactions, the CSM / MCA requests that only serious or unusual reactions be reported. Any reaction which is fatal, is life threatening, disabling, incapacitating, or which results in, or prolongs, hospitalisation should be reported, even if well recognised.[17] These data are especially of value when comparing drugs in the same class. Examples of 'serious' reports that are of particular interest to the CSM / MCA are listed in Box 1.2.

Box 1.2. Examples of serious reports specifically requested by the CSM / MCA

Anaphylaxis	Jaundice
Blood disorders	Hepatic abnormalities
Convulsions	Renal abnormalities
Endocrine disturbances	Ophthalmic disorders
Effects on fertility	Severe CNS effects
Haemorrhage from any site	Severe skin reactions

1.15 Problems with CSM / MCA data.

Although the data received by the CSM / MCA are of great value with regard to pharmacovigilance, there are limitations to their use (Table 1.2).[25] For example, reporting rates for drugs tend to be at their highest following their introduction onto the market, particularly as they are marked with black triangles. Furthermore, owing to underreporting and because the number of patients taking a drug is unknown, it is impossible to calculate the incidence of specific

ADRs and it is only possible to hypothesise about identified problems. It is not uncommon for unusual or unexpected reactions to be reported at the expense of well recognised, albeit more serious, reactions.

Table 1.2: Strengths and weakness of the Yellow Card Scheme. (Taken from Drugs 1999; 57 (4): 527)

Strengths of scheme	Weaknesses of scheme
• A nation-wide reporting scheme • Monitors a drug for its entire marketed life • Potential for all reactions to be reported for all patients • Provides a means for detecting rare ADRs • Allows monitoring in all practice areas • Allows for comparison of drugs with similar indications or similar drug classes.	• Many reactions are clearly not drug-related • Many reactions are never reported • Biases exist in reporting for example, severity or seriousness of reaction, ease of recognition of reaction, novelty of drug, promotion and publicity given to drug or adverse reaction, extent of use of drug, and / or reporting of reaction • Cause and effect relationship with drug cannot be established • Does not allow for assessment of incidence because the number of reactions and number of patients who received and took the drug are not known.

1.16 Other methods of pharmacovigilance.

More robust or systematic methods employed in pharmacovigilance include case control studies, cohort studies and case register studies. These methods, rather than relying on spontaneous reports, focus on individual drugs with the aim of identifying ADRs. For example, the Prescription Event Monitoring (PEM) Scheme was developed at the University of Southampton and is designed to target particular drugs.[28] Alternatively, these studies focus on selected clinical conditions to identify potential relationships with individual drugs.

1.17 Classification of ADRs.

Traditionally, ADRs have been classified into two distinct categories (Table 1.3). 'Type A' reactions tend to be extensions of a drug's pharmacological effects while 'Type B' reactions tend to be more bizarre in nature as they are idiosyncratic, unpredictable and unrelated to the pharmacological action of a drug. Currently, this classification is under review, primarily because the two groups are somewhat restrictive. Further subtypes of ADR that could be created are those caused by long term use of a drug, those caused by drug-drug interactions, ADRs resulting in carcinogenicity or teratogenicity and ADRs occurring as a result of an overdose.

Table 1.3: Classification of adverse drug reactions

Reaction type	Nature of reaction	*Example of reaction type*
Type A	These reactions may be predicted from the pharmacological actions of the drug and are usually dose-dependant. They tend to be mild, have low mortality and may be alleviated by a reduction in dose.	*Dry mouth with anti-cholinergics, hypoglycaemia with anti-diabetics*
Type B	These reactions are unpredictable from the pharmacology of the drug and are not dose-dependent. They have a higher mortality rate than Type A reactions.	*Anaphylactic reactions to penicillin, hepatotoxicity with sulphasalazine.*

1.18 Role of clinical pharmacists

Pharmacists are establishing themselves in roles that go far beyond the days when the manufacturing, compounding and dispensing of medicines were *the* roles for pharmacists. As clinical pharmacy began to evolve, drug history taking, drug information, patient counselling and education and, ward-based clinical pharmacy emerged as examples of this developing role. Many definitions of

clinical pharmacy exist but inherent in all of them, is that pharmacists are concerned with the safe and effective use of drugs. Indeed the concept of pharmaceutical care, which had a huge impact on the concepts surrounding these developing roles, is defined as "a practice in which the practitioner takes responsibility for a patient's drug related needs and holds him or herself accountable for meeting these needs".[27] Included in this concept were the problems associated with adverse drug reactions. It was not surprising therefore that pharmacists began to look towards pharmacovigilance as a role in which they, 'the experts on drug therapy', could make a substantial contribution.

While pharmacists may not posses the diagnostic skills of doctors, the clinical component of undergraduate and postgraduate courses means that pharmacists are now well equipped to cope with complex pharmacology and therapeutic problems.[28] These skills may be used in the prediction, identification or prevention of adverse drug reactions. Ward pharmacists are well placed to identify and report ADRs. This may be achieved through interaction with medical staff, ward staff and patients. Identification of certain clues such as the sudden discontinuation of maintenance therapy, or prescriptions for medicines that may be used to treat ADRs, for example corticosteroids or anti-histamines, may suggest the occurrence of an ADR.[29] The possibility that ward pharmacists could identify ADRs in this manner was demonstrated in the early 1980s.[30]

Outside the United Kingdom, pharmacists were involved in post marketing surveillance schemes, but within the UK, this was not the case. A proposal by the RPSGB to initiate pharmacists reporting via a 'Pink Card' scheme was rejected by a CSM / MCA and Committee on Dental and Surgical Materials

and vaccines, and any reaction to a new drug (marked with the black triangle symbol▼). A report may be made where there is a reasonable suspicion of an ADR; definite proof is not required. An education pack, "Pharmacovigilance, The Yellow Card Scheme: Information Pack for Pharmacists", containing details of the reporting protocol and information concerning the Yellow Card Scheme was sent by the CSM / MCA to each hospital pharmacy premises in the demonstration areas. The CSM / MCA RMCs provided workshops about this new role on a national basis in summer / autumn 1997.

The potential role of community pharmacists in pharmacovigilance has also been explored.[36] Although it has been demonstrated that community pharmacists are able to identify and report ADRs, the studies were not carried out as part of the Yellow Card Scheme. In April 1997, the CSM / MCA established a demonstration scheme for community pharmacists to report ADRs via the Yellow Card Scheme in the four CSM / MCA RMC areas.[37]

1.20 The role of pharmacists in pharmacovigilance abroad.

Pharmacists have been recognised as reporters in official, post marketing surveillance schemes for a number of years in many other countries.[38] In America, pharmacists have been able to report ADRs as part of MedWatch since its inception. It has been reported that ADR reports submitted by pharmacists to this scheme are of a high quality and that countries disregarding the potential of hospital pharmacist reporting should consider changing their practice.[39] The American Society of Health-System Pharmacists suggests that pharmacists should exert leadership in the development, maintenance and

ongoing evaluation of ADR programs.[40] It also states that pharmacists have a 'responsibility and professional obligation to report any suspected ADRs'. This advice and guidance appears to have been effective as, in 1992, hospital pharmacists were the most frequent direct reporters of ADRs to the Food and Drug Administration.[41] In Australia, pharmacists are recognised reporters in the Adverse Drug Reactions Advisory Committee (ADRAC).[42] In the early 1980's, it was reported that nearly half of the ADRs received by ADRAC were from hospital pharmacists.[42] In Canada, pharmacists have also been involved in the Canadian Drug Adverse Reaction Reporting Program (CDARRP).[43] Like MedWatch, the program is a voluntary spontaneous reporting scheme and pharmacists play a significant part in its operation.

In Canada, Australia and the USA, the associations concerned with hospital or health system pharmacists have produced guidelines on the importance of pharmacovigilance, how pharmacists should become involved in pharmacovigilance and what their role should be. In the United Kingdom, this support has not been provided.

Chapter 2:

Local adverse drug reaction reporting schemes

Chapter 2: Local adverse drug reaction reporting schemes

2.1 The pharmacist's role in local schemes.

Pharmacists have been instrumental in setting up ADR reporting schemes and are integral to their operation.[44,45] Such activity provides pharmacists with an opportunity to interact with other health care professionals and patients, and to become directly involved in the monitoring, management and evaluation of ADRs.

2.2 Hospital-based local adverse drug reaction-monitoring schemes.

The problem of under-reporting of ADRs and its effect on pharmacovigilance has been partly addressed in the United States of America where hospitals are required by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) to have procedures for reporting ADRs.[46] This is also the case in Australia where the Australian Council on Healthcare Standards (ACHS) requires hospitals to operate such schemes.[47] In the United Kingdom, although such a requirement does not exist some hospitals have set up in-house or local ADR reporting schemes.

Local ADR reporting schemes in current operation are not designed to replace the Yellow Card Scheme but to supplement it by increasing awareness and encouraging reporting of ADRs within hospitals. Local schemes also aim to minimise the factors discussed earlier which may deter potential reporters from making an ADR report (see Box 1.1).[19,20,21] A number of examples of local reporting schemes have been published in the literature and although methods of reporting may vary between institutions, most operate on similar principles (Box 2.1).[44,48,49,50,51,52]

Box 2.1: Requirements for the operation of a typical local ADR reporting scheme
Identified operators of the scheme
System for reporting (card, telephone, computer)
Feedback to reporters
Centre for collation of reports
Information sources to research and evaluate ADRs
Funding
Multidisciplinary involvement and co-operation

2.3 ADR reporting at the Royal Liverpool University Hospital.

In 1985, a local scheme was introduced at the Royal Liverpool University Hospitals (RLUH), the 'Green Card' scheme.[44] Still in operation, the scheme has resulted in an increase in the number of ADR reports to the Pharmacy department and a subsequent increase in reports to the CSM / MCA.[53] However, if the reported incidences of ADRs experienced by hospital in-patients[3] and ADR related hospital admissions[4] are compared to the number of patients treated by the RLUH each year, under-reporting of ADRs remains a cause for concern in the hospital.

'Green Cards' are available on all wards and clinics, and with few details required can be completed by any member of the hospital staff and sent to the pharmacy department. Yellow Card reports are more complex, difficult and time consuming to complete which has been shown to have an adverse effect on reporting rates. 'Green Cards' used at the RLUH and similar cards in other local schemes tend to be

more basic in their design that makes it faster and simpler to report an ADR. A number of variations on the 'Green Card' exist, and examples of information required to be included on such cards are shown in Box 2.2. A 'Green Card' used at the RLUH is provided in Appendix 5.

Box 2.2: Details required for locally designed ADR report card or for telephone reporting

Patient name

Patient hospital ID number

(Addressograph if possible)

Location of patient

Name of suspect drug(s)

Details of suspected reaction(s)

Name of reporter

Status of reporter (profession)

Contact number / address

Factors which facilitate the operation of a program such as the 'Green Card' scheme are listed in Box 2.3.

Box 2.3: Factors facilitating the operation of a local ADR reporting scheme

Low cost

Simple to operate

Easy to maintain

Easily available in patient areas (for example wards, clinics and casualty departments)

Minimum impact on pre-existing workload

Highly visible

Constantly publicised

At the RLUH, once the pharmacy department has received a report, either the drug information pharmacist or ward pharmacist retrieves the patient's medical records. An ADR investigation form is completed including patient details, concurrent illnesses, vital organ function and known drug allergies (Box 2.4). The investigation form also provides information for completion of Yellow Cards should a report be appropriate.

Box 2.4: Details be included in ADR report form on review of patient medical records

- ♦ Patient age, sex (pregnancy) and weight (if appropriate)
- ♦ Medication details including:
    - ♦ Dose, route of administration, duration of therapy, indication
    - ♦ Drug allergies
    - ♦ Previous exposure to the drug(s)
    - ♦ Details of self medication
- Biochemical / haematological status (where relevant)
- Reason for admission
- Other illnesses
- Details of the reaction including:
    - ♦ Whether symptoms resolved on drug withdrawal or dose reduction
    - ♦ Whether re-challenge was performed
    - ♦ Whether corrective treatment was prescribed
    - ♦ Timing of the reaction after exposure
- Whether the patient's medical condition could have contributed to the ADR.
- Outcome

The appropriate literature sources (Box 2.5) are examined for previous reports of the reaction and details entered onto the ADR research form. The ADR team comprising the Drug Information Pharmacist and a Senior Registrar in Clinical Pharmacology then reviews the completed report. The ADR is evaluated and a decision is made determining the likelihood (or causality) that the suspect drug

caused the reaction. Clinical judgement is used to determine causality at the RLUH, however, an alternative method may be the use of algorithms. These algorithms consist of a series of questions concerning the circumstances surrounding the ADR which when evaluated, give an indication of the likelihood that the reaction was or was not an ADR. A variety of algorithms have been published of which Naranjo's appears to be the most commonly cited as it is reasonably reliable and simple to use.[54,55,56,57]

Box 2.5: Examples of literature sources for researching ADRs

- CSM / MCA (ADROIT database)
- British National Formulary
- Compendium of Data Sheets and Summaries of Product Characteristics
- Martindale: The Extra Pharmacopoeia
- Medline
- The Internet
- Meyler's Side Effects of Drugs
- Davies' Textbook of Adverse Drug Reactions
- Industry / Pharmaceutical Manufacturers
- Royal Pharmaceutical Society of Great Britain
- Specialist centres, for example, children's hospitals
- Drug Information Centres

Severity of reaction is also important as it often determines whether a report is submitted to the CSM / MCA. Use of clinical judgement to determine severity of reactions may be appropriate although categories of reaction severity are well

defined in the literature.[48,57] Reactions at the RLUH are categorised as 'serious' or 'non-serious' in accordance with CSM / MCA criteria (see 1.14).

In conjunction with whether the suspect drug is in the black triangle▼ category or if the reaction is 'serious' or unusual, a decision is made as to whether a report to the CSM / MCA is appropriate. Reports are then allocated a reference number and filed. Following evaluation of the report, an acknowledgement letter is sent to the reporter giving details of their report, whether a Yellow Card was sent to the CSM / MCA and a brief summary of previous similar reports where appropriate.

At the RLUH, a number of methods of providing feedback to potential ADR reporters are used. These include publicising the success of the scheme through committee minutes, the hospitals 'Drugs And Therapeutics' committee newsletters, pharmacy department newsletters and directorate memorandums. The scheme is further promoted via staff training sessions and promotional talks all of which are important methods of raising awareness of the scheme and hopefully, increasing reporting rates.

2.4 Reporting at other institutions.

Similar schemes are in operation or have been in adopted in other institutions. At the John Radcliffe Hospital, Oxford, locally designed Yellow Cards have been placed at the end of each patient's bed with the intention of eliminating the problem of locating cards to make an ADR report. Cards were checked each day by the ward pharmacists and although no longer in operation, the scheme was successful in generating an increase in the number of Yellow Cards.[46,58]

Retrospective coding of patient's pathologies during in-patient episodes by medical records has also resulted in identification of ADRs. This was achieved by retrospective review of patients' medical records and prescription charts for evidence that an ADR has occurred and also by identifying patients' records endorsed with coding (for example, International Classification of Disease (ICD) codes) signifying the occurrence of an ADR.[59,60] Telephone models have been developed to facilitate reporting of ADRs.[51] The advantage of reporting by this method is that no forms are required and telephones are readily accessible on most wards and clinics. Participants may prefer personal contact and where relevant, may have the opportunity to obtain advice from the drug information department concerning the suspected ADR. In other hospitals, schemes have been implemented in the outpatient setting with encouraging results.[51] Report cards may also be placed in other areas of the hospital, for example, casualty departments or theatres.

For hospitals with limited resources or staff, it may be possible to adapt schemes so that a minimal impact is made on workload by altering current procedures. For example, adaptation of pharmacy intervention monitoring programmes to cover ADR monitoring may allow collection and collation of ADR data by pharmacists without greatly altering current practice.

2.5 Reporting of reactions to newly marketed agents.

Schemes to increase the reporting of ADRs to black triangle▼ drugs have been evaluated.[49,50] A scheme in which newly marketed drugs were highlighted by the use of 'sticky labels' placed on prescription charts was implemented at the Northern General Hospital, Sheffield.[50] Lists of these drugs were also circulated and the

scheme was publicised in the hospital's 'Drugs and Therapeutics' bulletins. Although the scheme failed to make a large impact on the number of Yellow Card reports, were the increases in reports to occur on a national level, then such initiatives may prove to be somewhat more worthwhile.

A similar study was conducted at the Nottingham City Hospital, resulting in an appreciable increase in the number of ADRs reported to the CSM / MCA via the Yellow Card Scheme.[49] In addition to the measures effected in the Northern General study, dispensed containers were marked with labels to highlight the fact that the drug was under intensive surveillance by the CSM / MCA.

2.6 The role of computers.

The future of adverse drug reaction monitoring will undoubtedly change as the role of computers in hospitals evolves. Computers are currently involved in biochemical, haematological, microbiological, prescribing, dispensing (including the detection of drug-drug interactions and potentially drug-disease interactions), medical information and administrative activities. Cross-referencing of these functions will provide a powerful tool with which to monitor the safety of drugs. Preliminary studies examining this aspect of ADR monitoring have already produced encouraging results.[61,62,63]

2.7 Use of data from local schemes.

Primarily, the data from local schemes have been used to contribute to national pharmacovigilance schemes. In-house, collation of ADR data may facilitate the identification of trends or problems which may be preventable or highlight the need for stricter monitoring of certain drugs. As a result of one study, digoxin fact sheets

were produced and placed in the appropriate patients' medication file. As a result of the same project, a limit of seventy two hours duration was placed on the use of parenteral ketoralac and information from the scheme resulted in deletion of oral ketoralac from the hospital formulary.[60] Changes in drug administration procedures, implementation of new prescribing policies, promotion of awareness of ADRs, modification of patient education procedures and drug ordering systems and therapeutic drug monitoring procedures were all implemented in some hospitals as a result of ADR data collected via local schemes.[64]

2.8 The importance of local schemes

There is no doubt that local ADR reporting schemes make a positive contribution to the identification and reporting of ADRs. A number of different models for reporting schemes have been published in the literature. Departments wishing to develop a scheme may choose whichever model may complement their clinical operations. Their design should overcome some of the problems associated with under-reporting and facilitate the development of an ADR reporting culture. The scheme must be continuously promoted and provision of feedback to reporters is essential. The schemes should also improve pharmaceutical care by identifying prescribing issues within hospitals, ensuring ADRs are processed effectively and efficiently and contributing to pharmacovigilance. Pharmacists are well placed and have the necessary skills with which to carry out these important functions. Formal involvement in the Yellow Card Scheme now means that pharmacists have a major role to perform in pharmacovigilance.

In order to investigate and assess the contribution pharmacists are making and could make to pharmacovigilance in the UK, this study was initiated.

Chapter 3:

Aims and objectives of the study

Chapter 3: Aims and objectives of the study

The previous chapters have described some of the limitations of spontaneous ADR reporting in the UK. Given that pharmacists' training is becoming increasingly clinically orientated, pharmacists have the potential to make a significant contribution to pharmacovigilance initiatives on a local and national basis. During the design of the program of studies for this thesis in 1996, pharmacists were not recognised as official reporters of ADRs to the Yellow Card Scheme. Thus, the initial focus of this thesis was to evaluate and identify roles for pharmacists in ADR reporting and an in local ADR reporting schemes. This was to be achieved using a national postal questionnaire survey and a prospective evaluation of the local ADR reporting scheme at the RLUH described in section 2.3. In addition, it was intended to conduct a prospective investigation of the problems associated with ADR-related admissions and an investigation of the potential for using computerised data to monitor and report ADRs. The results of these studies could then be used to identify potential roles for pharmacists.

The introduction of reporting for pharmacists described in section 1.19 and which took place in 1997 presented an opportunity to widen the proposed plan of research. The focus of this thesis therefore altered slightly to include an evaluation and assessment of pharmacists' involvement in and contribution to the Yellow Card Scheme using both qualitative and quantitative methodology. The initial survey of hospital pharmacy departments' involvement in ADR reporting was repeated to evaluate the impact that this development had on the operation of local or in-house schemes.

The overall aim of the thesis was therefore met by a series of related, but self-contained studies, which gradually built up a comprehensive picture of ADR reporting by hospital pharmacists in the UK.

Specifically, the aims of the thesis were:

1. **To identify hospital pharmacists' current involvement in ADR reporting.**

The objectives for this phase of the study were;

- To investigate and assess the involvement of hospital pharmacy departments in ADR reporting, and factors influencing the existence of local ADR schemes.
- To assess influences upon and the number of reports received by local ADR schemes.
- To ascertain the influence of the Yellow Card Scheme on hospital pharmacy departments' involvement in local schemes.

2. **To identify potential roles for hospital pharmacists in ADR reporting in in-house or local ADR reporting schemes.**

The objectives for this phase of the study were;

- To develop and evaluate a computer database to record, analyse and report ADRs.
- To assess methods of improving reporting rates of a local or in-house ADR reporting scheme.
- To investigate the transfer of data from secondary to primary care concerning ADRs that patients may have suffered while in hospital.

3. To investigate pharmacists attitudes to, and knowledge of ADR reporting.

The objectives of this phase of the study were;

- To ascertain the extent to which hospital pharmacists have become involved in ADR reporting.
- To assess pharmacists' attitudes to, and knowledge of, the Yellow Card Scheme and to compare it with those of medical staff assessed in previous studies.
- To identify pharmacists' concerns about the Yellow Card Scheme and to identify factors that could encourage pharmacists to report ADRs.

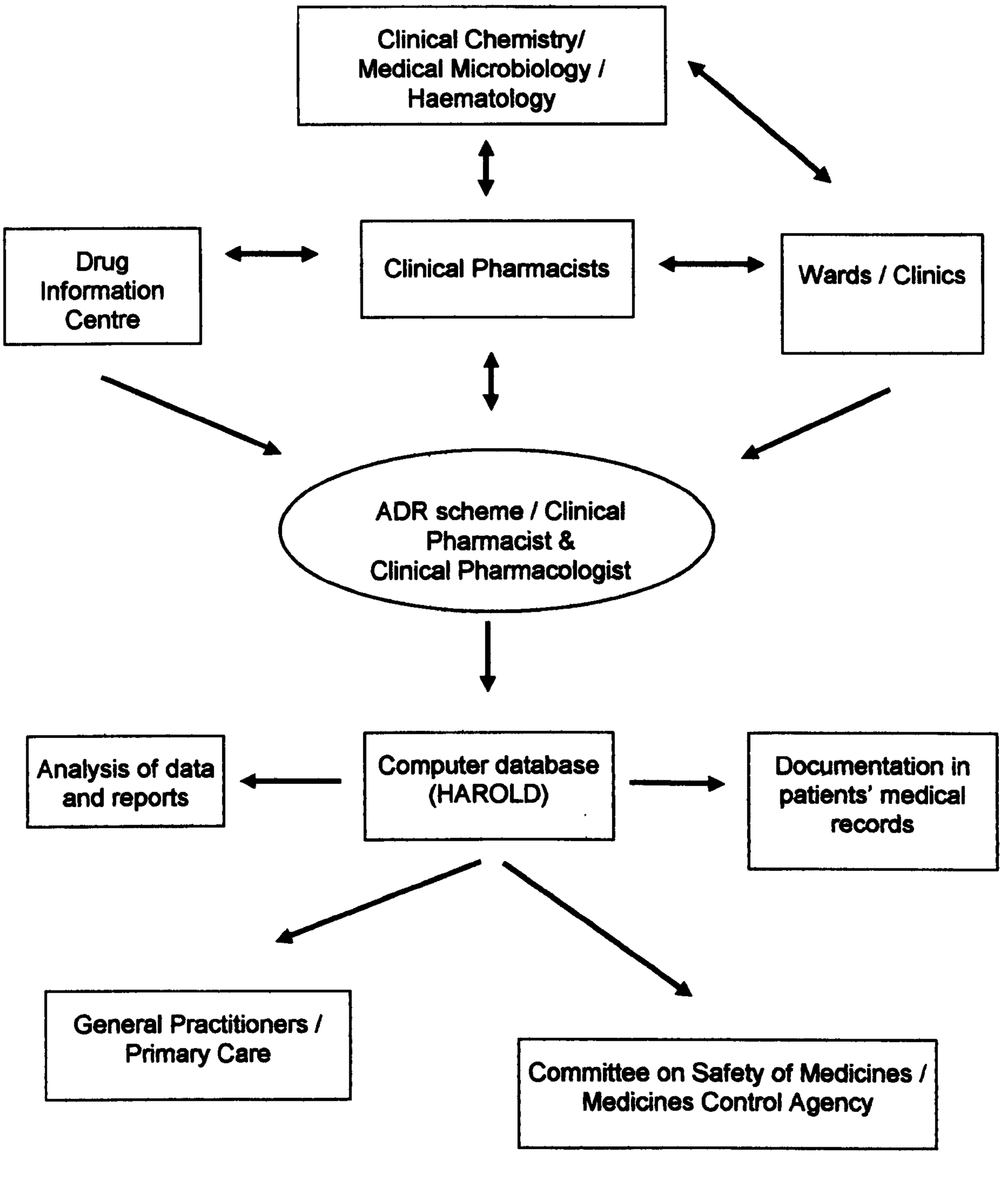
4. To investigate in areas in which ADRs have a significant impact and identify potential roles for pharmacists.

The objectives of this phase of the study were;

- To assess levels of reporting of ADRs for clinically significant ADRs in ADR-related admissions.
- To collate data about the nature of ADR-related admissions.
- To identify areas in which pharmacists could contribute to the reduction in impact and frequency of ADRs..

These four areas of research are closely linked to the model of clinical pharmacy practice in the UK. Such a model is illustrated in Figure 3.1 in which ADR-related activities are the focus.

Figure 3.1: Flow chart illustrating model of clinical pharmacy.



Chapter 4:

An investigation into adverse drug reaction reporting by hospital pharmacy departments in the United Kingdom.

Chapter 4: An investigation into adverse drug reaction reporting by hospital pharmacy departments in the United Kingdom.

4.1 Introduction

A number of examples of local reporting schemes have been published in the literature (see Chapter 2). Types of reporting system vary between institutions although most operate on the principle that reports are made to the pharmacy department using locally designed forms or by telephone.

The aim of this phase of the thesis was, by surveying randomly selected hospital pharmacy departments throughout the United Kingdom, to assess the extent of involvement of pharmacy departments in ADR monitoring schemes and to highlight innovative practices within such schemes.

4.2 Method

A questionnaire was devised, covering a wide range of issues including size of hospital and pharmacy departments, roles of pharmacists employed by departments, existence of ADR reporting schemes and where appropriate how such schemes operate. The questionnaire was piloted at 15 hospitals and as a result, minor alterations were carried out to the wording of the questionnaire.

Two hundred hospitals, out of an estimated 1000 hospitals in the UK, were selected at random from two databases. One hundred were selected from the United Kingdom Drug Information Pharmacists Group (UKDIPG) and a further one hundred from the directory in the Chemist and Druggist Annual (excluding

any hospitals selected from the UKDIPG).[65,66] Hospitals were selected from the UKDIPG as it was felt that hospitals with drug information facilities may be more likely to have ADR schemes and therefore provide more information about the methods used in operating such schemes.

The questionnaire, a covering letter (Appendix 1) and a prepaid envelope with which to return completed forms were sent to randomly selected hospital pharmacies in July 1996. Envelopes were addressed to the 'Clinical Services Manager' as it was felt that these individuals would be, in some respect, largely responsible for the operation of these schemes. For hospitals without a Clinical Services Manager, it was anticipated that the questionnaire would be completed by a pharmacist with clinical services input.

Questionnaires were distributed in July 1996 and were returned over the following two months. Returned questionnaires were entered onto a database and analysed using the Epi-Info Version 6.3.[67] Analysis of results included frequency evaluations, comparison of mean values and cross tabulations in which χ^2 tests were applied. P values of ≤ 0.05 were taken to be statistically significant.

4.3 Results

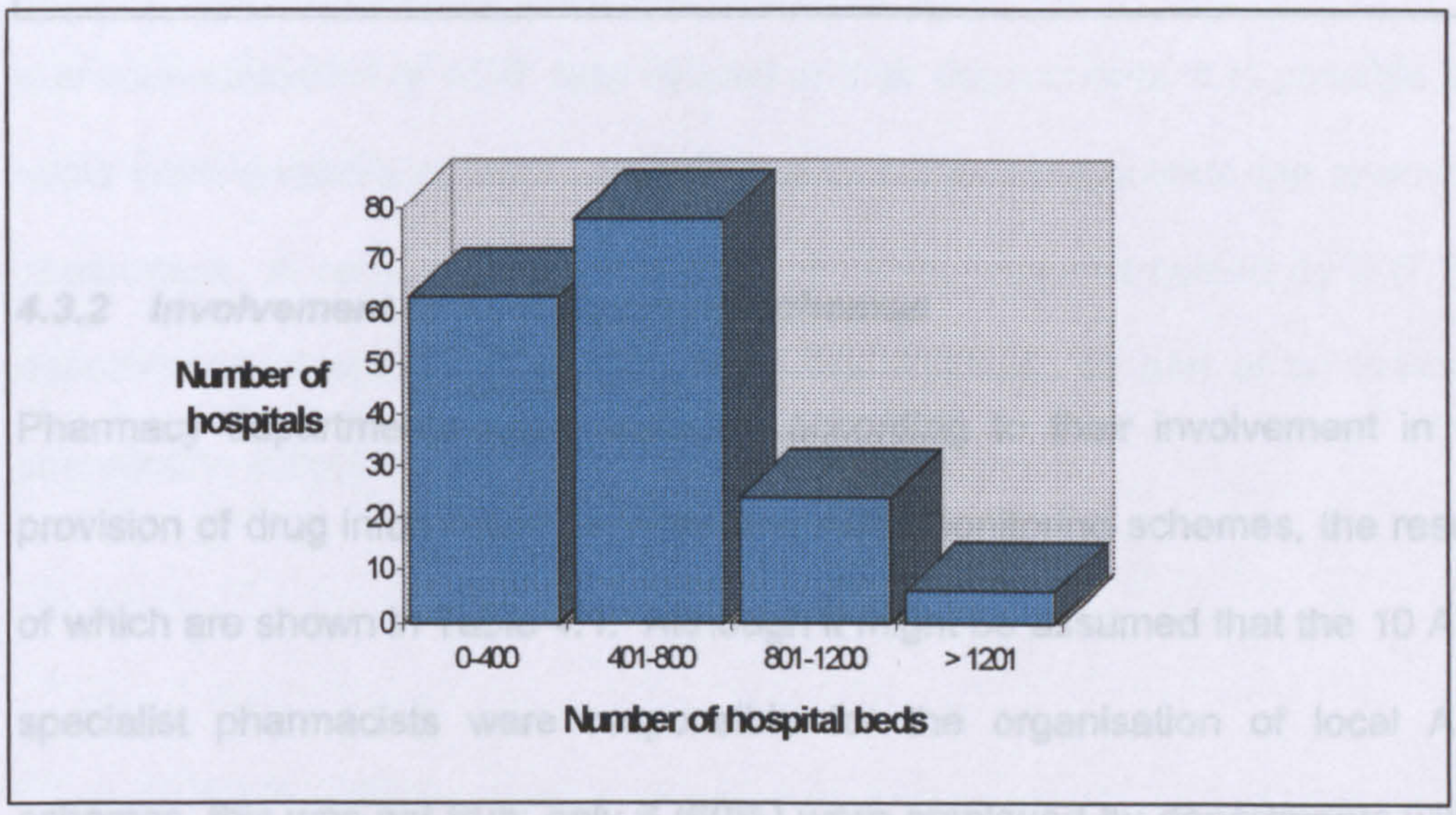
Of the 200 hospitals surveyed, 172 (86%) responded. No significant difference was observed in response rate from hospitals selected from the UKDIPG (84 responses (84%)) and those selected at random from the Chemist and Druggist register (88 responses (88%)) (χ^2=0.66, p=0.4). No significant difference

between the two groups was observed in terms of the number of pharmacists employed by each department (χ^2=5.45, p=0.14) and the number of departments operating a local ADR monitoring scheme (χ^2=0.8, p=0.2) although hospitals in the UKDIPG group tended to have a larger number of hospital beds ((χ^2=6.97, p=0.07). As expected, one significant difference was observed between the two groups, in that departments in the UKDIPG group were significantly more likely to have a Drug Information Pharmacist (χ^2=20.0, p<0.0001).

4.3.1 Surveyed hospital demographics

Distribution of the size of the respondent hospitals is shown in Figure 4.1.

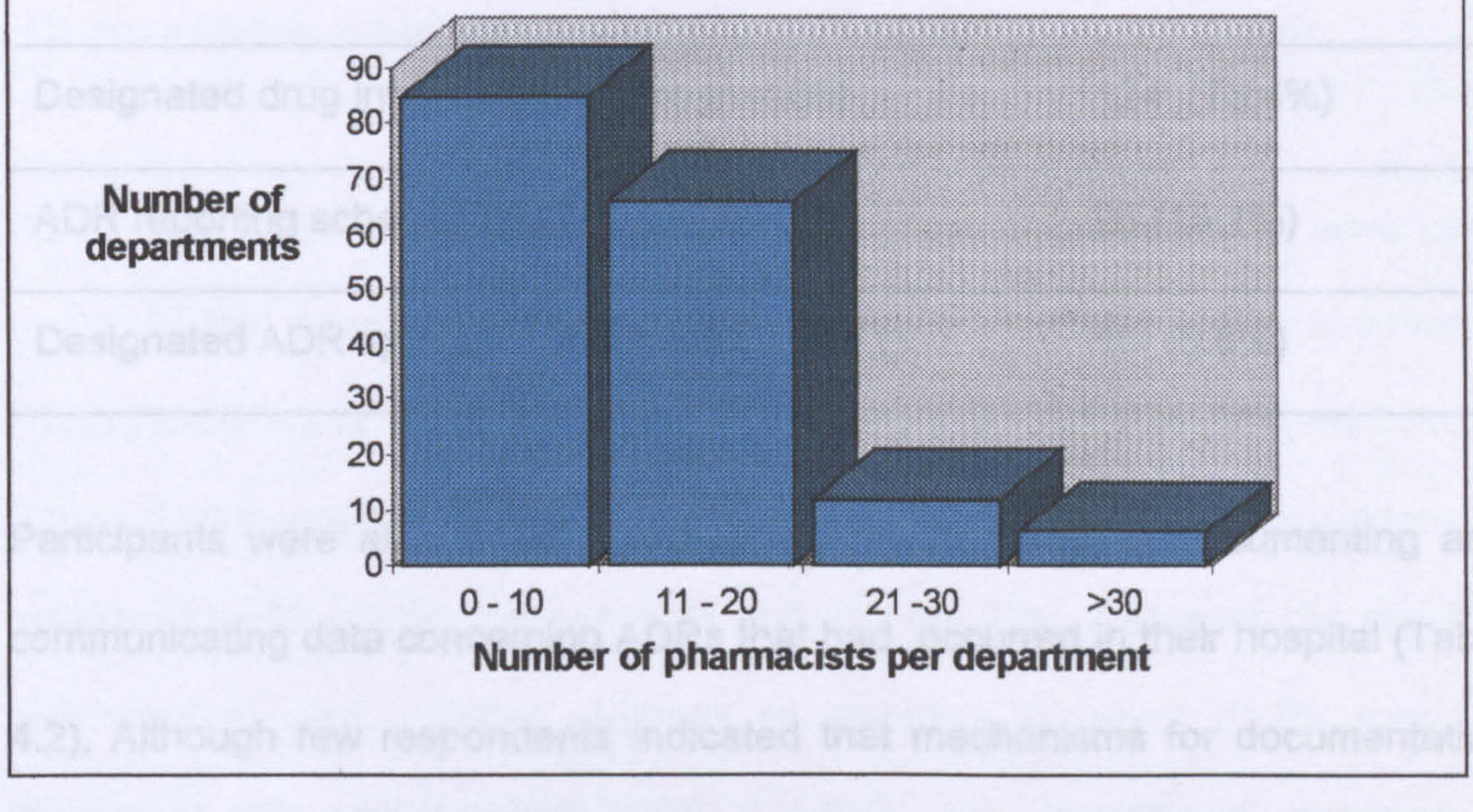
Figure 4.1. Distribution of hospital size (n=172)



Of these 172 hospitals, 102 (59.3%) were part of larger NHS trusts, 58 (33.7%) were affiliated to university medical schools and 27 (15.7%) had a Clinical Pharmacology department within the hospital. An ADR specialist nurse was

employed by 1 (0.6%) hospital. The distribution of the number of pharmacists employed by each department is shown in Figure 4.2.

Figure 4.2. Distribution of number of pharmacists per department



4.3.2 Involvement in ADR reporting schemes

Pharmacy departments were analysed according to their involvement in the provision of drug information services and ADR monitoring schemes, the results of which are shown in Table 4.1. Although it might be assumed that the 10 ADR specialist pharmacists were responsible for the organisation of local ADR schemes, this was not true; only 6 (60%) were employed by departments with a local ADR reporting scheme. The four who were not associated with local schemes were based in hospitals with drug information centres suggesting that this may have some association with their role.

Table 4.1. Activities related to Drug Information and ADR monitoring performed by surveyed departments

Activity (n = number of responses per question)	Number participating in activity
Designated drug information pharmacist (n=171)	131 (76.6%)
Designated drug information centre (n=169)	124 (73.4%)
ADR reporting scheme (n=172)	26 (15.1%)
Designated ADR specialist pharmacist (n=171)	10 (5.8%)

Participants were also asked about formal mechanisms for documenting and communicating data concerning ADRs that had occurred in their hospital (Table 4.2). Although few respondents indicated that mechanisms for documentation and communication of ADR data existed in their departments, it is possible that some were unaware of such mechanisms that may exist outside the pharmacy department. A computerised data base of ADRs, was maintained by 2 (7.7%) departments of which one hospital used the database as part of an in-house intervention collection.

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Table 4.2. Formal mechanisms of documentation and communication of details of ADRs (n=172)

Mechanism	Yes
Documentation in patients' notes	4 (2.3%)
Communication to patients' general practitioners	3 (1.7%)
Communication to patients' community pharmacists	1 (0.6%)

Data collection forms, for the purpose of evaluating identified ADRs, were used by 25 (14.5%) departments of which 16 (64%) were involved in a local scheme. Having identified an ADR, 2 (1.2%) respondents used an algorithm (see section 2.3) to decide whether to report an ADR to the CSM / MCA. Clinical judgement was used by 83 (48.3%) respondents and 157 (91.2%) discussed the reaction with medical staff. Other methods of deciding to report ADRs included discussion with senior pharmacists (1 (0.6%)) and reporting all reactions to unlicensed medicines (1 (0.6%)).

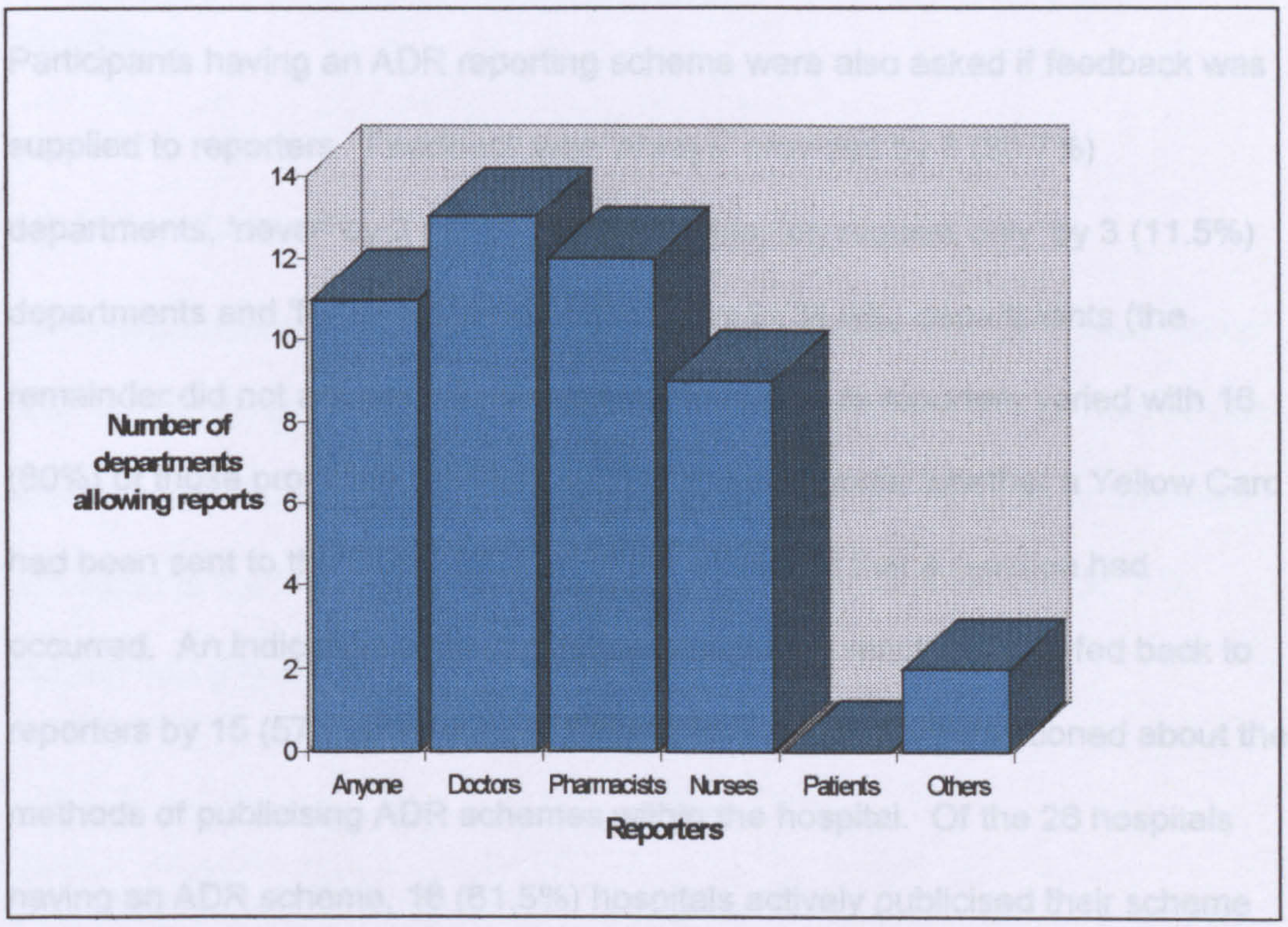
4.3.3 Hospitals having ADR reporting schemes

Of the 172 responding hospitals, 26 (15.1%) had an ADR reporting scheme. Schemes were organised by pharmacy departments in 21 (84%) cases, Clinical Pharmacology Departments in 2 (8%) cases and in single instances (4%), schemes were operated either by senior medical staff alone or by a combination of pharmacy and Clinical Pharmacology Departments.

Reports of suspected adverse drug reactions were made to pharmacy departments in a number of ways, with some departments using a combination

of methods. Locally designed cards were used by 16 (61.5%) departments, telephone reporting was used by 10 (38.5%) departments and CSM / MCA Yellow Cards were used by 8 (30.8%) departments. No other methods were reported. The CSM / MCA 'Yellow Card' category included 4 departments involved in the Northern Regional pilot scheme investigating participation in the Yellow Card Scheme by pharmacists.[21] Personnel allowed to report via such schemes differed between establishments (Figure 4.3). Some departments allowed reporting by 'Anyone', whereas some departments were more selective (see discussion).

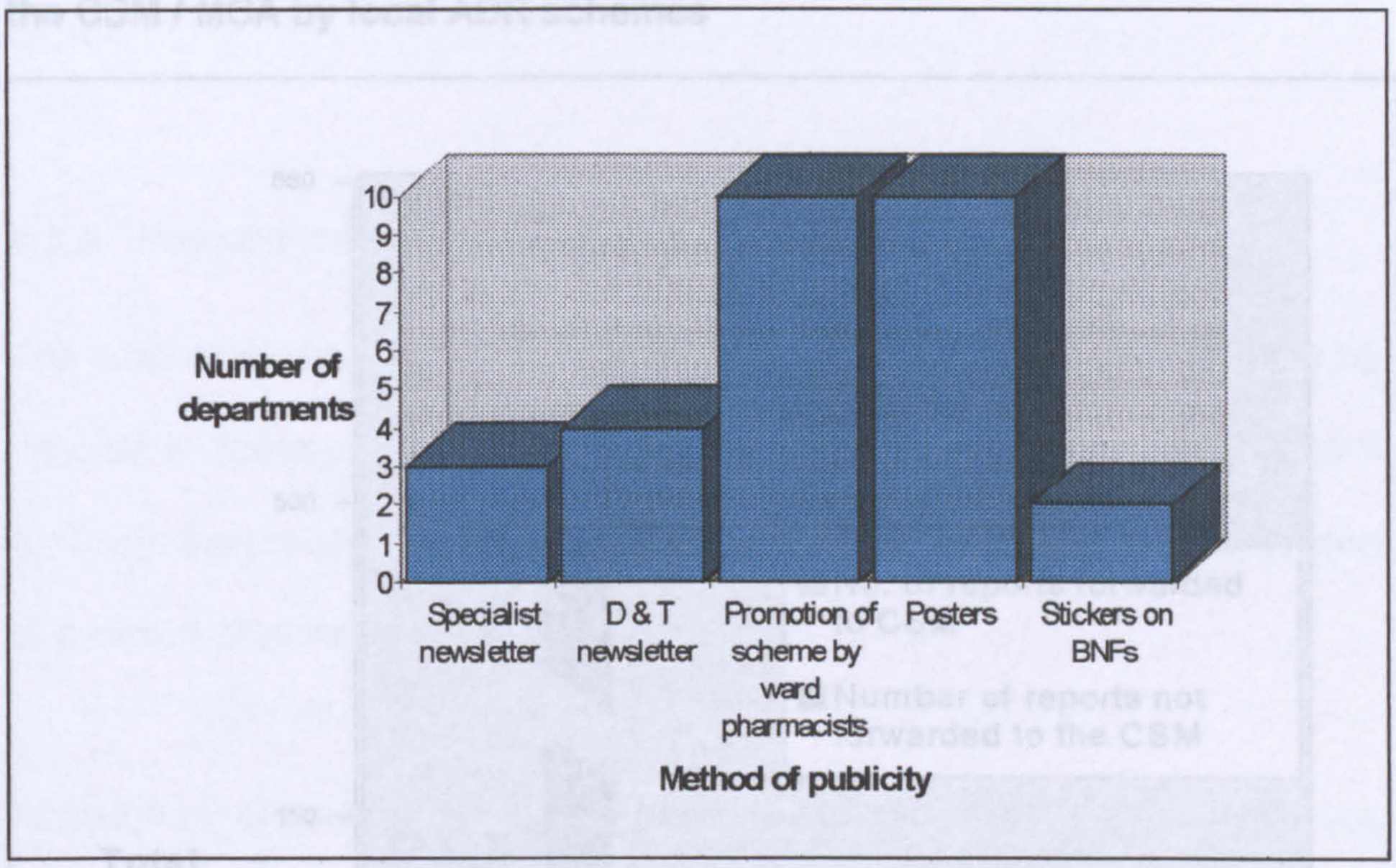
Figure 4.3. Staff groups permitted to participate in local ADR reporting schemes (n=26)



For those units using 'Yellow Card' reporting, pharmacists and other professions were not always included in these schemes as, at the time of the survey, only doctors and dentists were allowed to submit 'Yellow Cards' direct to the CSM / MCA with the exception of the Northern Regional scheme (see section 1.19). Hospitals were also asked, where possible, if they could provide examples of locally designed cards or ADR investigation forms. Cards were provided by 7 (26.9%) departments and ADR investigation forms were provided by 2 (7.7%) of hospitals. These cards tended to be similar in design with only basic information being required to make a report. Patient details, suspect drug, brief details of the suspected reaction and details of the reporter were required for most reports.

Participants having an ADR reporting scheme were also asked if feedback was supplied to reporters. Feedback was 'always' provided by 8 (30.7%) departments, 'never' by 3 (11.5%) departments, 'on request only' by 3 (11.5%) departments and 'for selected reports only' by 9 (34.6%) departments (the remainder did not answer). The nature of feedback to reporters varied with 16 (80%) of those providing feedback informing the reporter whether a Yellow Card had been sent to the CSM / MCA or of the likelihood that a reaction had occurred. An indication of the incidence of reported reactions was fed back to reporters by 15 (57.7%) schemes. Departments were also questioned about the methods of publicising ADR schemes within the hospital. Of the 26 hospitals having an ADR scheme, 16 (61.5%) hospitals actively publicised their scheme using methods described in Figure 4.4. Other methods of promoting the scheme included co-operation with clinical audit (1 (3.8%)) and lecturing to doctors during their induction week (1 (3.8%)).

Figure 4.4. Methods of publicising ADR schemes within hospitals (n=26)

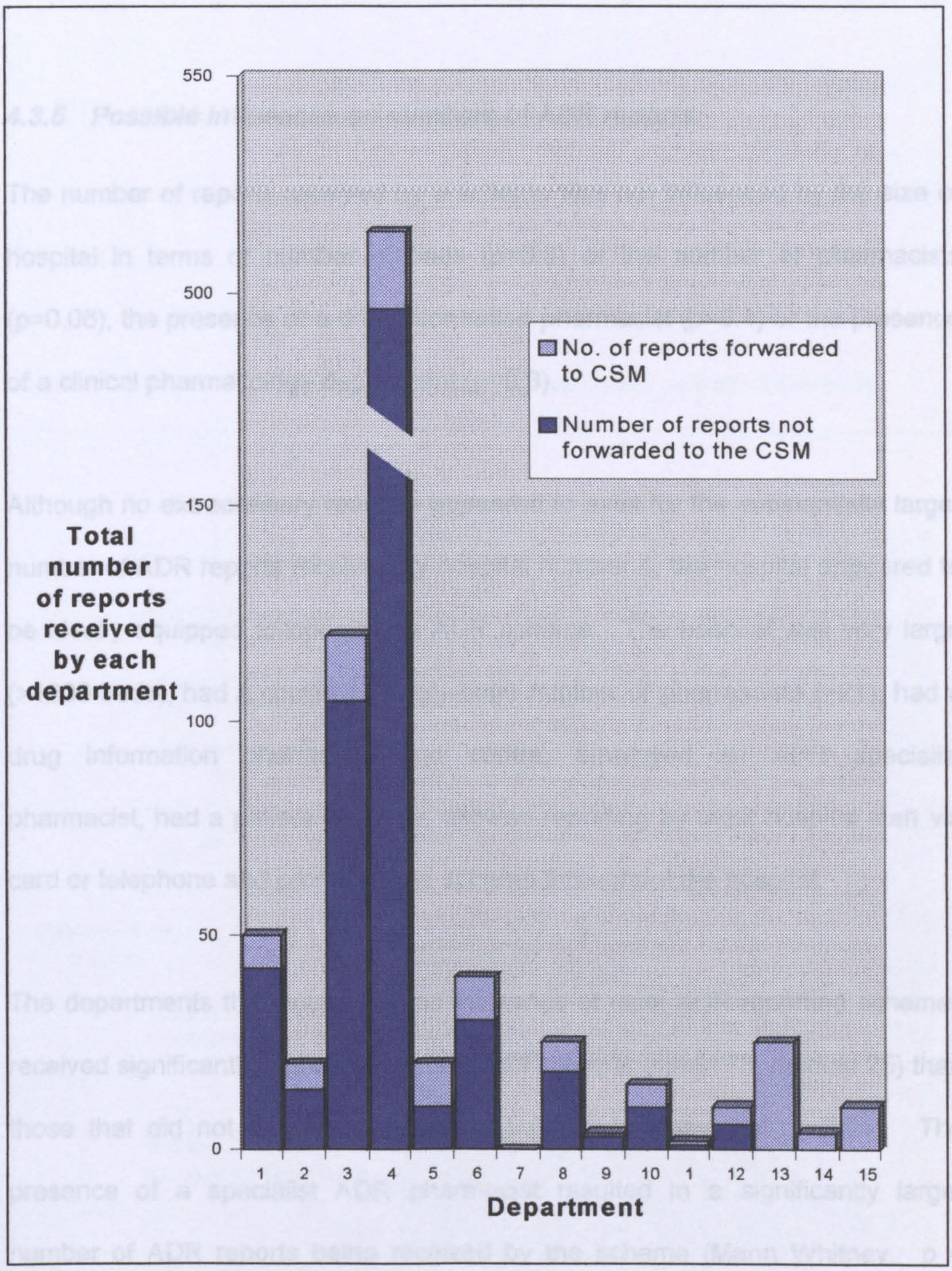


N.B. 'D&T' newsletter refers to hospitals' Drug and Therapeutics Committee newsletters

4.3.4 Numbers of ADR reports received by local schemes

Some respondents declined to state the number of ADR reports received each year. Of the 15 who did, the number of reports received each year ranged from 0-526 (mean 52.3± 115.3, median 20). Of these reports, the number that were submitted to the CSM / MCA each year ranged from 0-30 (mean 9.8± 8.5, median 9.0) (Figure 4.5).

Figure 4.5. Number of ADR reports received and subsequently forwarded to the CSM / MCA by local ADR schemes



Overall, just over one third of reports were forwarded to the CSM / MCA (mean 36.6% ± 30.5, range 0-100%, median 27%). Despite having a scheme, hospital 7 received no reports. For hospitals 13, 14 and 15 in Figure 4.5, Yellow Cards

were used to report ADRs and all reports were subsequently sent to the CSM / MCA.

4.3.5 Possible influences on numbers of ADR reports.

The number of reports received by a scheme was not influenced by the size of hospital in terms of number of beds (p=0.3) or the number of pharmacists (p=0.06), the presence of a drug information pharmacist (p=0.4) or the presence of a clinical pharmacology department (p=0.3).

Although no extraordinary reasons appeared to exist for the substantially larger number of ADR reports received by hospital number 4, the hospital appeared to be ideally equipped to operate an ADR scheme. The hospital was very large (>1200 beds), had a correspondingly large number of pharmacists (>21), had a drug information pharmacist and centre, employed an ADR specialist pharmacist, had a patient help line, allowed reporting by most hospital staff via card or telephone and promoted the scheme throughout the hospital.

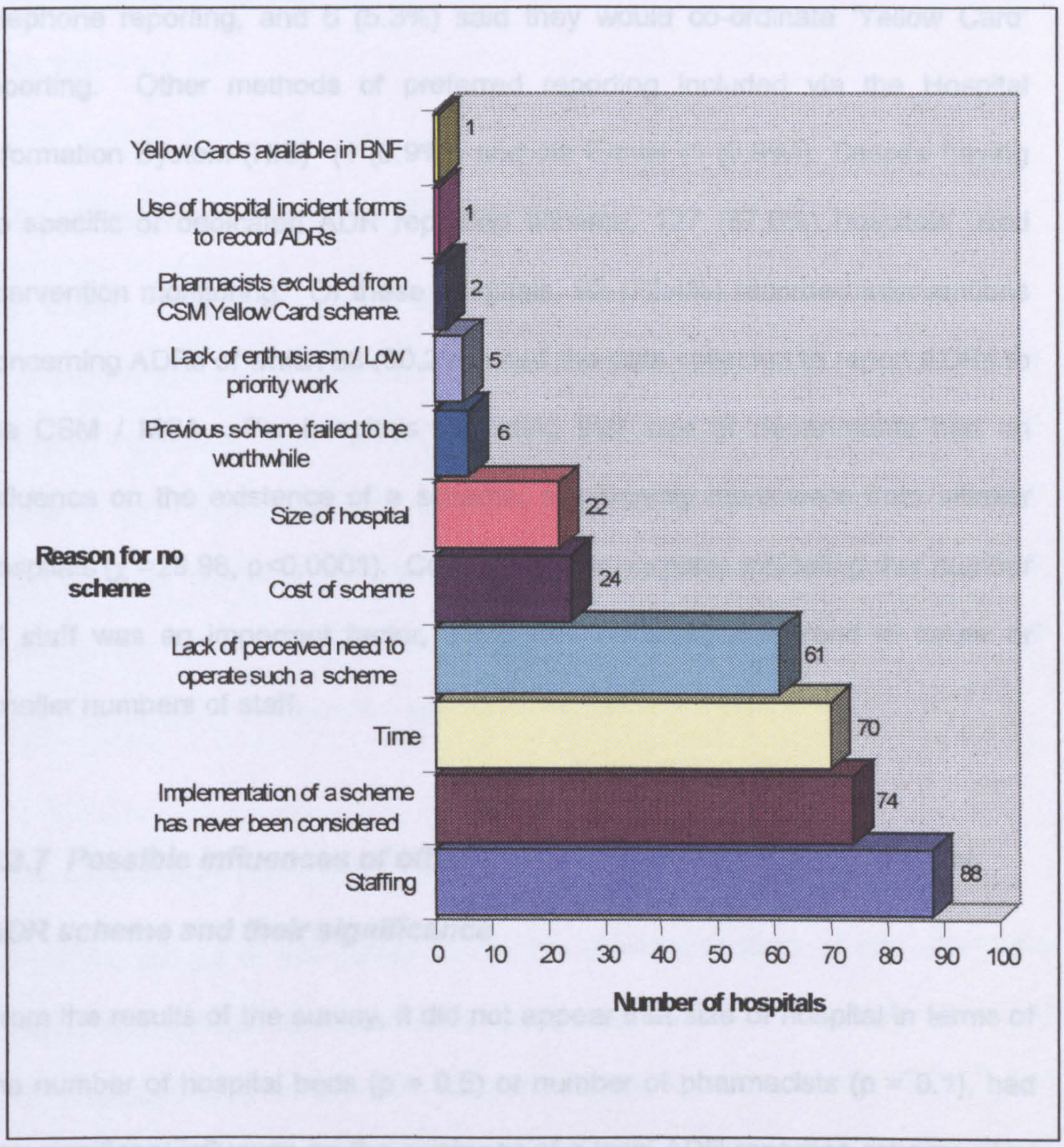
The departments that publicised the existence of local ADR reporting schemes received significantly higher numbers of ADR reports (mean 73; median 25) than those that did not (mean 14, median 5) (Mann-Whitney test, p=0.04). The presence of a specialist ADR pharmacist resulted in a significantly larger number of ADR reports being received by the scheme (Mann Whitney, p = 0.05). Those having an ADR pharmacist received a mean of 146 reports (median 50) in comparison to a mean of 21 reports (median 15) for departments without an ADR pharmacist. Hospitals providing feedback to reporters received

a significantly larger number of ADR reports (mean 73; median 25) than those not providing feedback (mean 13; median 5) (Mann-Whitney test, p=0.04).

4.3.6 Hospitals without local ADR reporting schemes

The reasons why hospitals did not have ADR reporting schemes are shown in Figure 4.6.

Figure 4.6. Reasons why a local ADR scheme does not exist (n=143)



Other reasons for the absence of a scheme included a hospital which used incident forms to record ADRs (1 (0.7%)), 'Yellow Cards' being freely available in BNFs (1 (0.7%)), and the fact that pharmacists were excluded from the 'Yellow Card' ADR reporting scheme (2 (1.4%)).

Of 146 departments having no scheme, 113 (77.4%) said they would consider implementing schemes in their hospital. Of these, 90 (79.6%) said they would utilise reporting by locally designed card, 66 (58.4%) said they would use telephone reporting, and 6 (5.3%) said they would co-ordinate 'Yellow Card' reporting. Other methods of preferred reporting included via the Hospital Information System (HIS) (1 (0.9%)) and via E-mail (1 (0.9%)). Despite having no specific or dedicated ADR reporting scheme, 127 (87.0%) hospitals used intervention monitoring. Of these hospitals, 92 (72.4%) recorded interventions concerning ADRs of which 83 (90.2%) used the data collected to report ADRs to the CSM / MCA. For hospitals indicating that size of departments had an influence on the existence of a scheme, significantly more were from smaller hospitals (χ^2=29.98, p<0.0001). Conversely, for hospitals indicating that number of staff was an important factor, there was no significant trend in larger or smaller numbers of staff.

4.3.7 Possible influences of other factors on the existence of a local ADR scheme and their significance

From the results of the survey, it did not appear that size of hospital in terms of the number of hospital beds (p = 0.5) or number of pharmacists (p = 0.1), had any significant influence on the existence of a local ADR reporting scheme. For

hospitals stating that number of staff was an important factor in relation to the absence of a scheme, there was no significant trend towards either larger or smaller numbers of staff (p=0.44). The hypothesis that the presence of a designated drug information pharmacist or centre would result in an increase in the proportion of hospitals having a scheme was not substantiated; in fact, a trend, although not significant (p=0.3), suggested the reverse. However, hospitals having a Clinical Pharmacology department were significantly more likely to have a local ADR reporting scheme in operation (χ^2=5.17, p=0.04) whilst a similar association was not true for hospitals affiliated to a medical school (p=0.15)

4.3.8 Monitoring of newly marketed agents

18 (10.4%) departments operated schemes to monitor adverse effects of newly marketed drugs, that is those marked with inverted black triangles in the British National Formulary, Data Sheet Compendium and on promotional material. Of these, 3 (16.7%) departments operated schemes in conjunction with a local ADR scheme. Methods of monitoring these drugs included highlighting them on prescription charts (13 (72.2%)), highlighting dispensing containers for these drugs (4 (22.2%)) and monitoring specific drugs for adverse effects (5 (27.7%)).

4.4 Discussion

From the results of the survey, it can be shown that there is less pharmacy involvement in ADR activities in the UK than in the US; 15% of this sample of UK hospitals were involved in ADR monitoring, compared with 80.7%[68] and 96%[69] of surveyed American hospitals in 1992. The American Society of

Hospital Pharmacists has taken a leading role in the development of pharmacy involvement with ADR reporting, publishing a number of articles and programmes to help pharmacists become more informed about ADR monitoring and reporting. As stated in Chapter 1, this approach appears to have resulted in hospital pharmacists becoming the most frequent reporters of serious ADRs to the FDA. Since the introduction of ADR reporting in the UK, the Royal Pharmaceutical Society of Great Britain is yet to offer a similar service to its members.

For hospitals with ADR reporting schemes, few major differences existed in the operation of local ADR reporting schemes. Most departments allowed more than one discipline to participate in their ADR scheme. It has been shown that different professions report different types of ADR.[70] A multi-disciplinary approach is therefore more likely to result in a larger quantity and wider variety of reports than one profession alone, particularly as it is not the responsibility of one individual to report an ADR that a patient may suffer.

It was unclear from the results of the study whether patients were allowed to participate in local schemes. The design of the questionnaire allowed respondents to indicate that either 'Anyone' could report via their local scheme or to indicate that patients or individual categories of hospital staff were allowed to report via their scheme by ticking the appropriate box. For those opting to tick individual professions rather than 'Anyone', none included 'Patients'. It is therefore possible that selection of 'Anyone' implied 'Any member of staff' rather than including 'Patients'. This may particularly be the case as 'Patients' may not have access to local reporting cards or telephone numbers in order to make an

ADR report. Nevertheless, patients are an important source of ADR information and should be encouraged to report suspicions of ADRs.

The results suggest that having a pharmacist to co-ordinate, operate and promote a scheme may increase the number of reports and raise the profile of the scheme. The nature and role of the ADR specialist pharmacist in hospitals which did not have an ADR reporting scheme was not clear. However, all 10 ADR pharmacists were from centres who had a drug information centre, which suggests some involvement in this area.

The most frequently used method of reporting was via locally designed card. 'Yellow Cards' were used by some departments although they may present some disadvantages in that they are more complicated to fill in than the local reporting cards obtained from this survey which are simpler to complete. Telephone reporting was also a frequently cited method and is also simpler to carry out than completion of a 'Yellow Card'.

Promotion of local schemes varied between departments and the more successful schemes tend to be those promoted within the hospital. Whether departments whose local schemes had collapsed due to lack of interest had effectively promoted their scheme within their hospitals is unknown. A lack of feedback concerning previously submitted ADR reports has been identified as a reason for failure of staff to report further ADRs. Most departments having an ADR scheme provided some degree of feedback to reporters. This acts as both feedback and promotion and may also inform participants in ADR reporting

schemes that their report is both appreciated and making a valuable contribution to surveillance schemes.

Some hospitals involved in the Northern Regional scheme stated that they did not have a local reporting scheme; conversely other hospitals in the same scheme stated that they did have a local scheme. This may be due to the subjectivity in which the answer to the question was decided upon or alternatively due to the degree of involvement of the departments in promoting the regional scheme and concurrent local ADR reporting activities within their hospitals or departments.

Reporting of ADRs to newly marketed drugs, that is, those marked with an inverted black triangle▼ is particularly important (section 1.13). The detection of rare ADRs, be it due to underlying pathology, drug-drug interactions, delayed onset or to their bizarre or unexpected nature, may not occur until long after the drug has been marketed.[71,72] As in-patients are a somewhat captive audience and biochemical and haematological data are often available for them, hospitals are therefore well placed to monitor for adverse drug reactions. Disappointingly few hospitals appear to be taking an active role in monitoring these drugs for ADRs. Although the use of many newly marketed agents is restricted by hospital formularies, many such agents are used by specialist centres before their use is widespread in general practice.

Few departments had any sort of formal documentation procedure for ADRs or any sort of formal communication procedure to patients' general practitioners. Furthermore, few hospitals had any sort of investigation form for the evaluation

of identified ADRs. ADR documentation and communication is left largely to the whims of those caring for the patient. Although it is expected that details of patients' ADRs would be documented in their medical records and communicated to their general practitioners via the discharge prescription and discharge letter, this is often not the case, even for more severe reactions.[73] ADRs should be processed correctly in order to protect the patient and prescriber from the effects of inappropriate re-exposure of the drugs concerned. Insufficient information may also prevent a patient being denied medications to which they have previously suffered minor adverse effects but could still be appropriately prescribed. Patients should also be informed of the name of the drug and the nature of their reaction as prescribers may not always have ready access to their medical records.

The results show that a large proportion of ADR reports are not forwarded to the CSM / MCA. This survey did not investigate reasons for this but it may be assumed that a large number do not satisfy the criteria defined by the CSM / MCA. A large number of reports are possibly not reported due to lack of information or uncertain causality. However, it would be of interest to investigate these reports to determine if common ADR reports appear and also if a significant number of reports that should be reported to the CSM / MCA are not being made.

Few departments used a computer to develop a database of ADR reports received by the pharmacy department. Such a database may be used to produce basic analyses of reports and to identify trends occurring within the hospital or frequent types of reaction. The database could also be programmed

to produce several reports from a single data set, for example, a letter for the GP giving details of the reaction, a label and letter for the patient's medical records, a report for the Drug and Therapeutics Committee and a report for the patient's community pharmacist (see Chapter 8).

Despite the fact that 84.9% of the hospitals in this sample did not have an ADR reporting scheme, a large number of departments indicated that they would consider implementing an ADR scheme. The proposed introduction of Yellow Card reporting for pharmacists (which was published after this survey was completed) may have prompted departments to introduce ADR reporting schemes and may have changed the attitudes of the many respondents who had said they would not consider implementing such a scheme and also those whose schemes had failed in the past.

For hospitals with limited resources or staff, existing activities may be altered to collect ADR reports. Telephone help lines for patients were under-used as methods of obtaining ADR data especially as they may be one of the few opportunities that patients may have to report ADRs. Intervention monitoring could also be used to a greater extent without greatly altering the methods or forms used to collect the necessary data and could be used as a form of reporting scheme for pharmacists within their own department.

Chapter 5:

Adverse drug reaction monitoring by United Kingdom hospital pharmacy departments: The impact of the introduction of Yellow Card reporting for pharmacists.

Chapter 5: Adverse drug reaction monitoring by United Kingdom hospital pharmacy departments: The impact of the introduction of Yellow Card reporting for pharmacists.

5.1 Introduction

The previous chapter described an investigation into the activities of hospital pharmacy departments in ADR monitoring in July 1996. This study was carried out at a time when hospital pharmacists were not allowed to report via the Yellow Card Scheme. Hospital pharmacists were invited to join the Yellow Card Scheme in April 1997. A follow up survey was undertaken in July 1998 to assess whether this change in practice had affected the extent to which hospital pharmacy departments were involved in in-house schemes and to further explore some of the issues addressed in the initial study.

5.2 Aim and objectives

The aim of the study was to assess the impact the introduction of Yellow Card reporting for hospital pharmacists had on the operation of local ADR reporting schemes. The objectives of the study were:

- to determine the number of hospitals having local schemes in comparison to the previous study
- to determine the number of reports received by these schemes and forwarded to the CSM / MCA in comparison to the previous study
- to identify methods by which the schemes operated
- to identify factors influencing whether hospitals operated a local scheme in comparison to the previous study

- to identify the number of reports received by schemes in relation to the number of pharmacists and the number of hospital beds in each hospital and to use this data as a marker of effectiveness of each scheme.

5.3 Method

A structured questionnaire was designed in which the issues addressed in the previous (1996) study were re-examined. The questionnaire was not identical to the one used previously; some questions were excluded and some new questions were included. Additional information sought included precise numerical data on the number of in-patient beds and pharmacists per hospital in order to calculate reports per bed and reports per pharmacist. Particular attention was paid to the operation of local ADR schemes and related activities and potential changes in the number of ADR reports made to the CSM / MCA by each pharmacy department. The issue of whether patients could report ADRs via local schemes, which the previous questionnaire failed to clarify, was also addressed. Since reporting had been introduced for pharmacists, the questionnaire asked for details of education and training that departments had carried out, in order to assess its impact on the numbers of reports made to the CSM / MCA.

In the previous study, one hundred hospital pharmacy departments had been selected from the UK Drug Information Pharmacists Group (DIPG) directory[65] and a further one hundred from the Chemist and Druggist Directory (C&DD) (excluding hospitals already selected from the DIPG).[66] Hospitals had been selected from the DIPG directory as it had been anticipated that hospitals with drug information departments might be more likely to have an ADR monitoring scheme and would therefore provide more data. In fact, this was found not to be the case.

The pre-piloted questionnaire, a covering letter and a pre-paid envelope was sent in July 1998 (16 months after the introduction of reporting by hospital pharmacists) to the same 200 hospital pharmacies as in the previous study (Appendix 2). Follow up letters and questionnaires were issued to non-respondents one month later. The questionnaire was addressed to the clinical services manager in each pharmacy department, as this approach in the previous study had resulted in an 86% response rate. For hospitals without a clinical services manager it was expected that the questionnaire would be completed by somebody with clinical input to the department's operation. Returned questionnaires were collated and evaluated using Epi Info version 6.3.[67] Analysis of results included frequency evaluations, comparison of mean values (± standard deviation) using the Mann Whitney test and cross tabulations in which chi squared tests were applied. $P \leq 0.05$ or less was selected to indicate statistical significance and all values were calculated at 95% confidence intervals.

5.4 Results

Of the 200 hospitals surveyed, 153 (76.5%) responded. Of these, three hospitals had been closed or had merged with another hospital since the previous study. These three were returned uncompleted and therefore excluded from the study. Therefore, of 197 possible responses, 150 (76.1%) responded.

5.4.1 Validity of results: comparison for the two surveys.

The response rate was 76.5%, a significant difference ($p=0.01$, $\chi^2 = 6.29$) in comparison to the response rate of the previous study (86% (172 / 200)). Overall,

there were no statistically significant differences in the demographics of the responding hospitals between the two studies. The size distribution of responding hospitals is shown and compared with the previous study in Table 5.1.

Table 5.1: Distribution of hospital size

Number of hospital beds	<400	401-800	801-1200	> 1200	Data not supplied
Number of hospitals '98 (n=150)	51 (34%)	67 (44.7%)	22 (14.7%)	7 (4.7%)	3 (2%)
Number of hospitals '96 (n=172)	63 (36.7%)	78 (45.3%)	24 (13.9%)	6 (3.5%)	1 (0.6%)

NB. Some percentages may not add up to more than 100% due to rounding up

The distribution of the number of pharmacists employed by each department is shown in Table 5.2. Of the hospitals responding, 45 (30%) were affiliated to a university medical school (58 (33.7%) previously), 19 (12.7%) had a Clinical Pharmacology department (27 (15.7%) previously) and 1 (0.7%) hospital had an ADR nurse (1 (0.7%) previously).

Table 5.2: Distribution of number of pharmacists per department

Number of pharmacists per department	< 10	11 - 20	21 - 30	>30	Data not supplied
Number of departments '98 (n=150)	73 (48.7%)	58 (38.7%)	8 (5.3%)	6 (4%)	5 (3.3%)
Number of departments '96 (n=172)	85 (49.4%)	66 (38.4%)	12 (7.0%)	6 (3.4%)	3 (1.7%)

NB. Some percentages may not add up to 100% due to rounding up

5.4.2 Comparison of DIPG and C&DD groups.

No significant difference in response rate was observed between the hospitals selected from the DIPG (76 / 150 responses, 50.7%) or from the Chemist and Druggist directory (74 / 150 responses, 49.3%). Comparison of the average number of hospital beds per hospital between the DIPG and C&DD groups revealed a similar profile (no significant difference) however, hospitals in the DIPG had a significantly larger number of hospital pharmacists (DIPG mean 13.8 ±8.9, C&DD mean 10.5 ±10.1, $p=0.001$). As expected, hospitals from the DIPG group were significantly more likely to have a drug information pharmacist ($p<0.001$, $\chi^2 = 21.51$). No significant difference was observed between the DIPG and C&DD groups with regard to the presence of a local ADR reporting scheme ($p=0.9$). Therefore, they can be analysed as a single sample for the purposes of this chapter.

5.4.3 ADR specialist pharmacists.

ADR specialist pharmacists were employed by 14 departments and hospitals having an ADR scheme were significantly more likely to have an ADR pharmacist than those without such a scheme (p=0.01, χ^2 = 5.78). Duties of ADR specialist pharmacists where hospitals had an ADR scheme included co-ordination of ADR reporting, education of staff, co-operating with clinical pharmacology departments and assessing ADR reports, whether alone or in conjunction with medical staff. In hospitals where ADR reporting schemes were absent, the roles of the ADR specialist pharmacists were similar and included education and training with regard to ADR reporting, co-ordinating data collection and queries about ADRs and responsibility for overseeing ADR reporting. Hospitals with an ADR pharmacist had a significantly larger number of hospital beds (mean 806.2, ± 420.0) in comparison to hospitals without (mean 546.2, ± 288.6, (p=0.03)). Similarly, hospitals with an ADR pharmacist had a significantly larger number of pharmacists (mean 21.8, ±18.1) in comparison to hospitals without (mean 11.2, ±7.6, (p=0.01)).

5.4.4 Involvement in ADR schemes.

The involvement of pharmacy departments in the provision of drug information services and ADR monitoring schemes is shown and compared with the previous study in Table 5.3. Telephone help lines for patients were operated by 41 (27.3%) hospitals and of these 17 (41.7%) departments used the help lines to report ADRs to the CSM / MCA.

Table 5.3: Pharmacy departments' drug information and ADR monitoring activities: Comparisons between surveys.

Activity / position	1998 (n=150)	1996 (n=172)	P value
Designated DI pharmacist	**79.3% (119)**	*+76.6% (131)*	0.6
Designated DI centre	**75.3% (113)**	**73.4% (124)*	0.7
ADR reporting scheme	***18.9% (28)**	*15.1% (26)*	0.4
Designated ADR specialist pharmacist	**9.3% (14)**	*5.8% (10)*	0.1

+ Data not supplied by one respondent
* Data not supplied by three respondents

Few departments (4 (2.7%)) had any procedures for documenting ADRs in patients' medical records. Only 1 (0.7%) department had any procedure for reporting ADRs to general practitioners (which involved a section on the discharge letter to explain the reasons for stopping drug therapy) and none of the departments had a procedure for communicating this information to patients' community pharmacists. A comparison with the previous study is shown in Table 5.4.

Table 5.4: Formal mechanisms of documentation and communication of details of ADRs. Comparison between surveys.

	1998 (n=150)	*1996 (n=172)*	P value
Documentation in patients' notes	**2.7% (4)**	*2.3% (4)*	0.8
Communication to patients' general practitioners	**0.7% (1)**	*1.7% (3)*	0.4
Communication to patients' community pharmacists	***0% (0)**	*0.6% (1)*	0.4

* Data not supplied in one response

5.4.5 Hospitals having ADR reporting schemes.

Of the hospitals surveyed, 28 (18.7%) stated that a local scheme was in operation, a non-significant increase in comparison to 26 (15.1%) departments in the previous study (p=0.6). There was no significant change in terms of which departments within hospitals organised local schemes. Of the 28 hospitals having a local scheme, 24 (85.7%) were operated by pharmacy departments only, 1 (3.6%) scheme was operated by clinical pharmacology alone and in 2 (7.2%) cases, the scheme was operated jointly between pharmacy and clinical pharmacology departments. The remaining hospital did not state who operated their scheme. To assess their quality or suitability for forwarding to the CSM / MCA as Yellow Cards, ADR reports were screened by 'pharmacists only' in 9 (32.1%) cases, 'pharmacists and medical staff' in 6 (21.4%) cases and 'medical staff only' in 2 (7.1%) cases. The remainder did not comment.

Reporting methods were similar to the previous study with some departments using multiple methods. CSM / MCA Yellow Cards were used by 11 (39.3%) departments, telephone and CSM / MCA Yellow Cards were used by 9 (32.1%) departments, locally designed cards, telephone and CSM / MCA reporting forms were used by 5 (17.9%) departments, 2 (7.1%) used locally designed cards only and 1 (3.6%) department used a combination of local cards and CSM / MCA cards. In comparison to the previous study, numbers of schemes using locally designed cards fell from 16 to 8 while those using CSM / MCA Yellow Cards increased from 8 to 27. Only one hospital had developed a computer database for their scheme, which was used to record and report on ADRs reported via the local scheme. The personnel allowed to participate in schemes varied between establishments. A notable difference between the present and the previous study was that pharmacists were now involved in all local schemes. An issue unclear from the first study was whether patients could report ADRs via hospital schemes. In this survey, of 28 respondents indicating that they operated a local scheme, 7 (25%) indicated that patients could report ADRs as part of a local scheme.

Feedback was provided to reporters by 25 (92.6%) of the 27 respondents who answered this question. Analysis and comparison of the numbers of reports received by departments who did and did not provide feedback were therefore of little value. Of the 25 departments, feedback was 'always' provided in 10 (40%) cases, 'on request' in 7 (28%) and 'for selected reports only' in 9 (36%). Of these, 7 (28%) respondents felt that providing feedback was 'very important', 13 (52%) 'important', 2 (8%) 'of little importance' and 1 (4%) 'of no importance'.

Local schemes were publicised by 16 (57.1%) of the departments having such programs. Methods included an ADR newsletter in 3 (10.7%) departments, Drug

and Therapeutics Committee Newsletter in 8 (28.6%), posters in 7 (25%) and stickers on the cover of BNFs in 1 (3.6%) hospital.

In response to an open question asking for general comments about their schemes, respondents appeared somewhat negative about the impact their schemes were having:

"Hoping to improve things with new DI pharmacist"

"Its rubbish really, we're too short staffed to do anything better"

"Plan to implement a better scheme"

"Present scheme not a great success, a more formal scheme may be better"

" Scheme not actively promoted due to staffing difficulties"

Other respondents reported that they promoted the existing Yellow Card Scheme rather than using locally designed cards:

"Not a local scheme as such, more a local procedure"

"DI collates Yellow Card reporting"

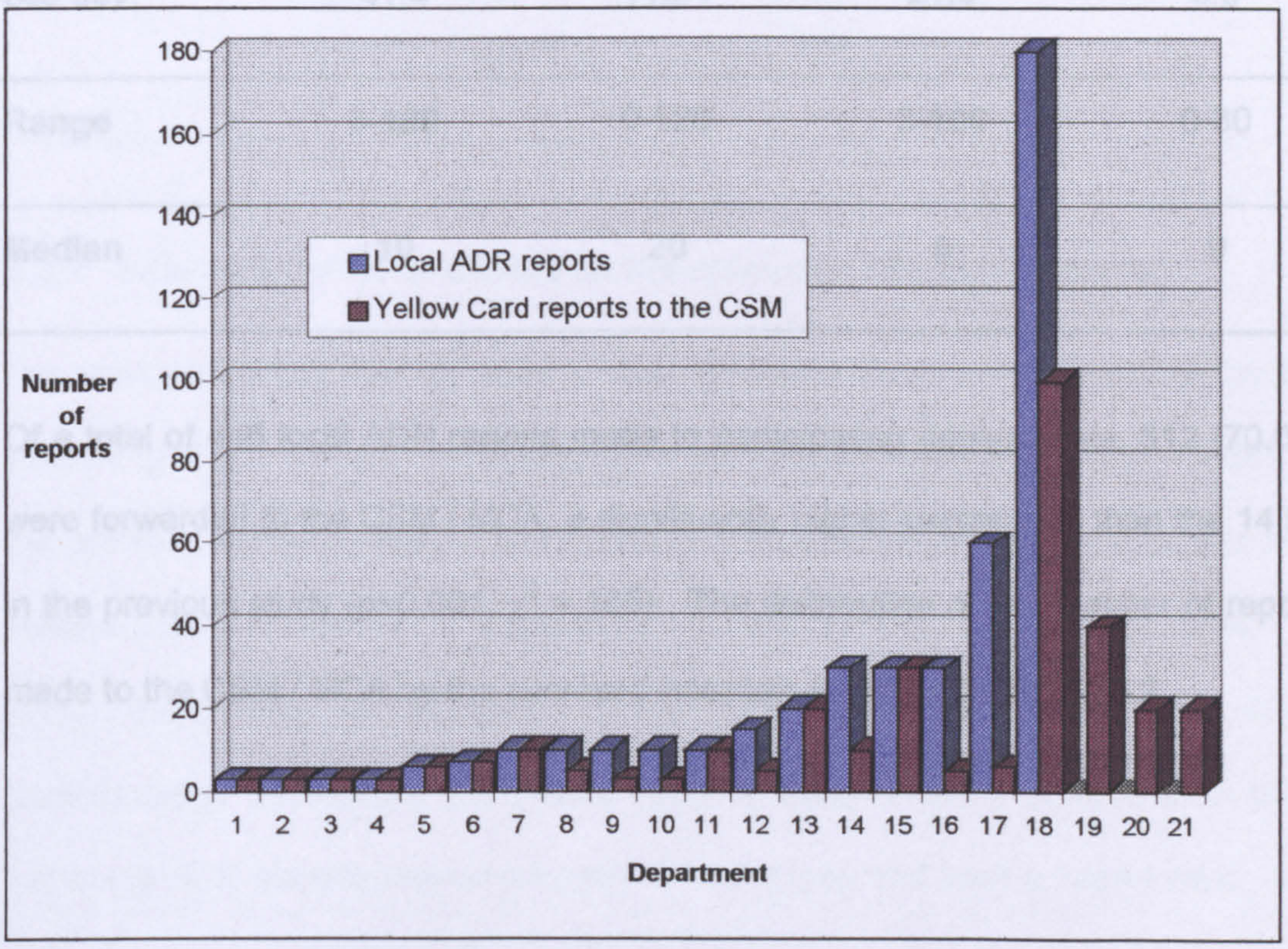
"Scheme generally acts to promote Yellow Card reporting to staff"

5.4.6 Numbers of reports received and made to the CSM / MCA.

Of the 28 departments having a local scheme, 18 provided details on both the number of local ADR reports and Yellow Card reports which they received and submitted to the CSM / MCA, while 3 departments only stated the number of Yellow Card reports they sent to the CSM / MCA. The number of local ADR reports ranged from 3 - 180 reports (mean 24.4, ± 42.6). In comparison to the previous study, the mean number of local ADR reports received by pharmacy departments was reduced from 52.3 ±112.7 in 1996 to 24.4 ± 42.6 reports in 1998, a non-significant difference

(Mann-Whitney, p=0.29). Local schemes received a mean of 0.02 local reports per inpatient bed per year (± 0.041, median 0, range 0 -0.15) and a mean of 0.01 CSM / MCA reports per inpatient bed per year (± 0.03, median 0, range 0 - 0.14). However, in the previous study, the mean number of reports per department was skewed by the fact that one hospital had received 526 local reports. No equivalent number was reported in this survey. Without this outlying figure, the mean values for local reports per pharmacy department in 1996 and 1998 were 26.8 (± 29.8) and 24.4 (± 42.6) respectively (p=0.4). Numbers of reports received by local schemes in this study are shown in Figure 5.1.

Figure 5.1: Numbers of ADR reports received by local schemes and reported to the CSM / MCA



Despite the fall in the number of local ADR reports received, a non significant increase was found in the number of Yellow Card reports to the CSM / MCA from a

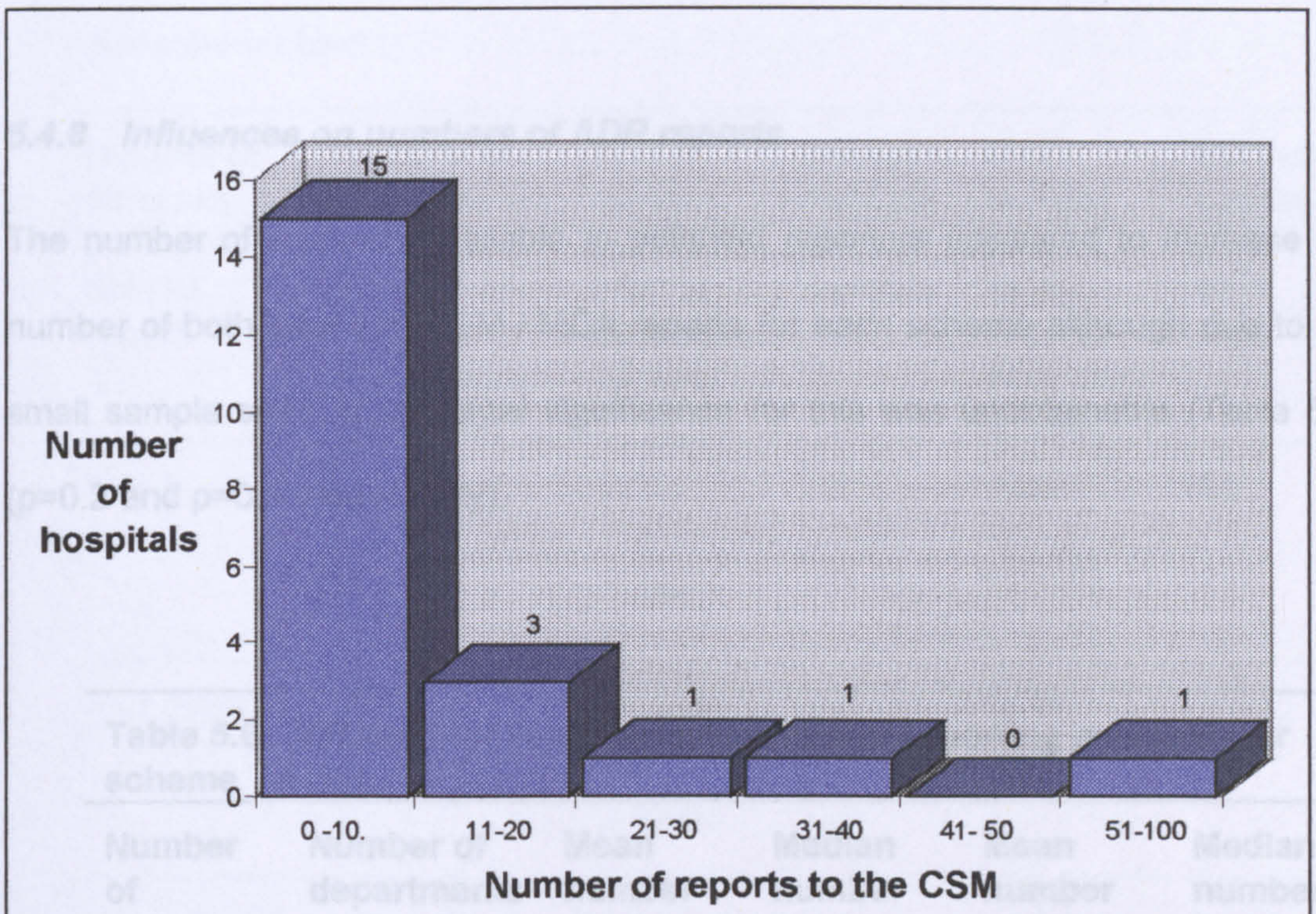
mean of 9.5, ± 8.2 reports in 1996 to a new mean of 15.3 ± 22.4 reports (range, 3 - 100) per department in 1998 (Table 5.5, p=0.8).

Table 5.5: Comparison of ADR reports made in 1996 and 1998.

	Local Reports		Yellow Card reports	
	1998 (n=21)	1996 (n=15)	**1998(n=21)**	1996 (n=15)
Total number of reports received by schemes	**4401**	1046	**312**	156
Mean number of reports received by schemes	**24.4**	52.3	**14.8**	9.8
Std dev.	**41.4**	115.4	**21.9**	8.5
Range	**3-180**	0-526	**3-100**	0-30
Median	**10**	20	**6**	9

Of a total of 446 local ADR reports made to participating departments, 312 (70.0%) were forwarded to the CSM / MCA, a significantly higher percentage than the 14.9% in the previous study ($p<0.001$, $\chi^2 = 165$). The distribution of the number of reports made to the CSM / MCA by the surveyed hospitals is shown in Figure 5.2.

Figure 5.2: Distribution of reports to the CSM / MCA



5.4.7 Influences of other factors on the existence of a local scheme.

Hospitals were more likely to have a local scheme if they were affiliated to medical schools ($p=0.03$, $\chi^2 = 4.61$) or a drug information pharmacist ($p=0.05$, $\chi^2 = 3.68$). In the previous study, neither of these factors appeared to influence the presence of schemes ($p=0.15$ and $p=0.3$ respectively). Unlike the previous study ($p=0.04$, $\chi^2 = 5.17$), there was no significant evidence that hospitals having a clinical pharmacology department were more likely to have an ADR scheme than those without ($p=0.3$) although fewer hospitals in this survey had such a department. ADR schemes were associated with larger hospitals as judged by the number of hospital beds (mean 820.6, $\pm$ 382.5) in comparison to hospitals without a scheme (mean 518.8, $\pm$ 264.1, ($p<0.001$)). Similarly, there was an association between hospitals with an ADR scheme and the total number of pharmacists in the department (mean

17.1, ±12.4 (p=0.003)) in comparison to hospitals without (mean 11.3, ± 8.6, (p=0.003)).

5.4.8 Influences on numbers of ADR reports.

The number of methods available to potential reporters appeared to increase the number of both local and CSM / MCA reports for each scheme although due to the small sample sizes, a statistical significance for this was unobtainable (Table 5.6) (p=0.2 and p=0.6 respectively).

Table 5.6: Influence of increasing numbers of reporting methods per scheme (n=18).

Number of reporting methods used.	Number of departments	Mean number of local reports (Standard deviation)	Median number of local reports	Mean number of CSM / MCA reports (Standard deviation)	Median number of CSM / MCA reports
1	11	12.0 (± 10.1)	10	9.6 (± 8.4)	7
2 or 3	7	44.0 (± 62.9)	22	20.7 (± 30.2)	6

There was no significant difference in the number of reports received by schemes in terms of the number of professions of staff available to report, although the mean number of local reports was higher in the group allowing three or more professions to report. (Table 5.7).

Table 5.7: Influence of increasing numbers of professions able to report per scheme (n=21)

Number of different professions able to report	Number of departments having number of different professions reporting	Mean number of local reports (Standard deviation)	Median number of local reports	Mean number of CSM / MCA reports (Standard deviation)	Median number of CSM / MCA reports
1 or 2	11	11.6 (± 8.8)	10	14.0 (±12.1)	10
3 or more	10	37.3 (± 56.5)	10	15.8 (±30.0)	5

Publicising schemes through Drug and Therapeutics Committee newsletters or posters and stickers on BNFs resulted in a increase in the numbers of local reports received by schemes (mean number of reports 38.2, ± 60.3, median 10) in comparison to those who did not (mean number of reports 13.4, ±10.3, median 10) although this difference was not significant. Publicising schemes also appeared to increase in the numbers of CSM / MCA reports received by schemes (mean number of reports 20, ± 28.7, median 7) in comparison to those who did not (mean number of reports 9.2, ± 9.1, median 5) although similarly, this difference was not significant.

5.4.9 Hospitals without an ADR reporting scheme.

Hospitals without a scheme were asked to respond about any future plans to introduce schemes in their departments and hospitals. Of the 120 respondents, 15 (12.5%) said they had definite plans to introduce a scheme in their hospital, 40 (33.3%) had probable plans to introduce a scheme and 65 (54.2%) said they had no plans to introduce a scheme. Responses correlated significantly with the number of staff within the department ($p=0.01$). Those having 'definite' plans to introduce a scheme employed a mean of 19.1 pharmacists, those having 'probable' plans employed a mean of 11.6 pharmacists and those with 'no' plans employed a mean of 9.3 pharmacists. The presence of a drug information pharmacist significantly increased the likelihood that a scheme would be adopted ($p=0.05$, $\chi^2 = 5.84$). However, the presence of an ADR specialist pharmacist did not ($p=0.5$).

5.4.10 Monitoring of newly marketed agents.

Of the 150 respondents, only 8 (5.4%) hospitals had schemes for monitoring newly marketed or black triangle drugs. Of these, 6 highlighted these drugs on prescription charts and 4 departments marked the containers in which these drugs were dispensed. Lists of these drugs were circulated to either the hospitals wards or to their pharmacists by 2 of the eight departments. Schemes had been implemented by 2 (1.4%) other departments but had been abandoned due to their ineffectiveness.

5.4.11 Education and training.

Of the departments responding, 94 (62.3%) had arranged education or training activities on adverse drug reaction monitoring for their departments. Of these, 79 (83.1%) had organised workshop or discussion sessions, 77 (81.9%) had distributed

the CSM / MCA information pack to pharmacists, 23 (24.5%) had held formal lectures and 7 (7.5%) had initiated local schemes and discussed issues relating to their implementation. Representatives of 4 (4.3%) departments had been sent to regional study days on the introduction of ADR reporting for pharmacists.

Those departments with greater numbers of pharmacists (mean 14.0 ± 10.3) tended to organise education or training activities compared with those with fewer pharmacists (mean 8.6 ± 6.2) not having such sessions ($p<0.001$). All but one department who provided information on the numbers of local and CSM / MCA ADR reports processed per scheme had organised education and training. Other significant influences on education and training activities included the presence of a local scheme ($p<0.001$, $\chi^2 = 12.44$), specialist ADR pharmacist ($p=0.02$, $\chi^2 = 4.98$) and a drug information pharmacist ($p=0.03$, $\chi^2 = 4.88$).

5.5 Discussion

This study was conducted to evaluate the impact that the introduction of reporting via the Yellow Card Scheme by hospital pharmacists has had on the operation of local or in-house ADR reporting schemes. In the previous study, 80.1% of respondents from hospitals without a local scheme said they would consider introducing a local scheme. Clearly the introduction of hospital pharmacist reporting did not provide the impetus for such developments (although in this study, 12.5% of those responding said their departments had 'definite' plans to implement a scheme and 33.3% had 'probable' plans). Furthermore, schemes that have been introduced have been unsuccessful in generating large numbers of ADR reports.

In the United States of America, operating ADR reporting schemes is a requirement for hospitals to become accredited with the Joint Commission on the Accreditation of Healthcare Organisations.[46] Furthermore, pharmacists have been allowed to report as part of the Food and Drug Administrations spontaneous reporting system "MedWatch" for a number of years. Similar research has demonstrated that 80.7%[68] and 96%[69] of surveyed American hospitals operated local or in-house schemes compared to 18.9% departments within this survey, a difference explained by the above reasons. However, it is clear that the importance of ADR monitoring has a lesser profile in the United Kingdom.

There have been no innovations in the methods by which ADRs are reported via local schemes; however, the results suggest that increasing the number of methods available improves reporting rates. The fact that 11 (39.3%) departments of the 28 having a local scheme used CSM / MCA Yellow Cards alone, and comments received concerning their operation, suggest that some departments are using these cards as part of a local procedure rather than locally designed scheme. This could also explain the increase in the proportion of reports forwarded to the CSM / MCA, that is, reports are only made in the first place if the reporter considers them appropriate for reporting as a Yellow Card report to the CSM / MCA, unlike some schemes where reporters are asked to report any suspected reaction.[12] These 'procedures' primarily involved co-ordination of Yellow Card reporting either by the hospital as a whole or by the pharmacy department itself. Such a scheme would place minimal demands on the department, encourage and increase awareness of reporting and reduce duplication and paperwork. In addition, the increase in the proportion of Yellow Cards submitted to the CSM / MCA could be due to a change in the proportion of reports originating from hospital pharmacists; however, this information was not collected as part of this study. Nevertheless, it is encouraging

that the number of Yellow Card reports submitted to the CSM / MCA has increased, albeit non-significantly. Staffing difficulties within the NHS further compound the problem of underreporting of ADRs in hospitals with local schemes.[74] While healthcare professionals are working in pressured environments, staff are forced to prioritise their work and as ADR reporting has no imediate gain to the patient at that time, it is possible that it is neglected for more pressing activities.

From the small numbers of departments allowing patients to report, it is clear that patients have very little opportunity to report ADRs without directly consulting a doctor or other healthcare professional. Other research has shown that patients are concerned about ADRs (potential or actual) and that they were the most frequently cited reason for calling a medicines information help line.[75] The Consumers Association has also voiced concerns about the public's awareness and ability to participate in ADR reporting schemes.[76] It is important that some provision is made for patients to enquire about or report ADRs to healthcare professionals in a position to give them appropriate advice and that these reports are used to promote drug safety.

Reporting of ADRs to newly marketed drugs, that is, those marked with an inverted black triangle▼, is particularly important given the limitations of clinical trials. The detection of rare ADRs, be they due to underlying pathology, drug-drug interactions, delayed onset or to their bizarre or unexpected nature, may not occur until long after the drug has been marketed.[71,72] It was somewhat disappointing that little activity had developed in the monitoring of the black triangle or newly marketed agents in the two years since the initial survey. Given the paucity of ideas concerning methods of monitoring these agents, it is improbable that any major inroads in this area will develop in the near future. The increasing use of computer assisted

prescribing may provide a solution to this, in that reporting processes can be built in to such programs prompting prescribers to report suspicions of ADRs.

Underreporting of ADRs was once again identified as a problem affecting local schemes. The combined number of inpatient beds for those hospitals having a reporting scheme was 22,156 beds. If the average inpatient episode lasts between one to two weeks, then it is not unreasonable to assume that this could account for up to or over one million patients treated at these hospitals each year. Assuming the data provided by Lazarou *et al*[4] correct and can be applied to this sample, if 6.7% of these patients have suffered a serious ADR then the 410 local ADR reports received over a year by local schemes represents a small fraction, far less than 0.1% of the potential 'serious' ADRs that might be reported to the local schemes and an even smaller fraction of those reactions which were reported to the CSM / MCA. This is substantially lower than previous estimates of the extent of under reporting.[16] Less than two thirds of departments had provided any sort of education or training activities concerning ADR reporting for pharmacists and this could have contributed to the lack of reporting

There had been no change in the number of hospitals having systems in operation to record ADRs in patients medical records and report them to either their general practitioner or to their community pharmacist. This is perhaps particularly surprising given the growing importance that many institutions are currently attaching to 'risk management' and clinical governance.[77] Although it is expected or assumed that details of patients' ADRs are documented in their medical records and communicated to their general practitioners via the discharge prescription and discharge letter, this is often not the case, even for more serious reactions.[73] Not surprisingly, general practitioners also perceive this transfer of information as

inadequate.[78] Patients and prescribers should be protected from the effects of inappropriate re-exposure of the drugs concerned. Alternatively, patients may be mistakenly denied medication to which they have previously suffered adverse effects but could still be appropriately prescribed in a situation where other drugs may be less suitable or effective.[79,80,]

Issues concerning quality within the NHS are currently increasing in importance as the concept of clinical governance gains momentum. Some studies evaluating the impact of ADRs have concluded that many ADRs are predictable and preventable.[81,82] Data from local ADR schemes could be used to evaluate the impact ADRs have on quality within hospitals or similar healthcare institutions. Since organisations are to be accountable for "continuously improving the quality of their services and safeguarding high standards of care", monitoring of ADRs to assess their impact has been defined as a key area. The National Institute for Clinical Excellence (NICE) is intended to set standards concerning the management of clinical situations and the utilisation of clinical interventions in which the management of ADRs would appear to be a core issue.[20] Furthermore, as reporting to the CSM / MCA is confidential, it is not possible for hospitals to collate data concerning ADRs within their institution without some in-house system for collecting and collating reports.

Chapter 6:

Attitudes of hospital pharmacists to adverse drug reactions and the Yellow Card Scheme: A qualitative study.

Chapter 6: Attitudes of hospital pharmacists to adverse drug reactions and the Yellow Card Scheme: A qualitative study.

6.1 Introduction

A review of the first year of reporting demonstrated that reports submitted by hospital pharmacists had made a valuable contribution to the Yellow Card Scheme. In terms of the quality of reports, significantly fewer required follow up by the CSM / MCA than those reports submitted by hospital doctors However, the numbers of reports submitted by hospital pharmacists had been somewhat lower than expected.[83]

6.2 Aims

The aim of this study was to investigate the attitudes of hospital pharmacists to ADR reporting, to identify any concerns they may have about this new role and to assess their attitudes to the CSM / MCA and the Yellow Card Scheme.

6.3 Methods

All major hospitals (n=13) within the Mersey CSM / MCA RMC catchment area were contacted and asked for permission to interview three clinical pharmacists. Chief Pharmacists were first contacted by letter outlining the purposes and nature of the study. Departments were then contacted by telephone to arrange a convenient time for face to face interviews if permissable.

Interviews were focused on subject areas which were incorporated into a semi-structured questionnaire (Appendix 3). The questionnaire was based on similar research tools examining the attitudes of community pharmacists[84] and medical

practitioners[20,21] to ADR reporting and was designed to assess pharmacists' attitudes to the Yellow Card Scheme, reporting of ADRs, reasons why they may not report ADRs and to assess their concerns about this new role.

Interviews were piloted on five hospital pharmacists from outside the RMC and the structure amended prior to the main data collection phase of the study. Some closed questions were changed to open questions and some questions were clarified. The same individual interviewed all pharmacists with interviews lasting approximately thirty minutes. The interviewer, who had previous experience in this methodology, prepared for the interviews through training sessions and literature review.[84]

Interviews were tape-recorded and transcribed into a word processing package, Microsoft Word, then exported to and analysed using WinMax Pro.[85] This program facilitates the collation of data using code words, categories or phrases with the intention to identify themes and issues raised during the interviews. Examples of code words or phrases include "black triangle drugs", "CSM / MCA", "Education and training", "Under-reporting" and "increasing reporting". These themes and issues are illustrated using verbatim quotes.[86] Two assessors carried out analysis individually and then jointly. Each interviewee was assigned an interview number for purposes of analysis and reporting comments (P1 - P38).

6.4 Results

Demographics of interviewees. Interviews were completed with 38 pharmacists from 13 hospitals (in one hospital, only two pharmacists were available for interview). Interviewees had been qualified for a mean of 8.1 years (± 6.6 years, range 1-30 years). Of those interviewed, 8 (21.1%) were currently undertaking diplomas in clinical pharmacy, 15 (39.5%) had completed a diploma in clinical pharmacy of whom 6 had extended their studies to MSc, while 11 (28.9%) had no postgraduate qualifications. 'Other' miscellaneous qualifications were held by 4 (10.5%) pharmacists. The interviews covered a wide range of issues and themes concerning the Yellow Card Scheme and a wide range of opinions and viewpoints were elicited from the interviewees.

6.4.1 Attitudes towards the current Yellow Card Scheme for reporting ADRs.

The Committee on Safety of Medicines. The CSM / MCA was criticised by a few interviewees for its lack of user friendliness or customer orientation:

P25: "I think they're a classic government organisation, its not easy to get through to the right person at the right time. They should adopt more of a pharmaceutical industry, medical information type approach, where there is always somebody available to take a call. They're typically a government organisation and not enough customer focused."

Widespread dissatisfaction with the manner in which the CSM / MCA had resisted pharmacist reporting was expressed. The idea that pharmacists were

allowed to report ADRs because numbers were dropping rather than because of their professional capabilities was expressed:

P4: "I was a bit peeved in a way that pharmacists were not regarded as competent enough to fill some form of ADR report."

P14: "I think the idea of getting pharmacists to report was because the number of reports had gone down, rather than them saying, "we'll let pharmacists report because they'll be really, really good at it"."

A few pharmacists appreciated the CSM / MCA's concerns about pharmacist reporting:

P8: "I could see where they where coming from in certain ways. You know, I could see that they have a vested interest as well, in not being swamped with masses of information which is of a dubious nature...."

Pharmacists felt that the CSM / MCA could encourage reporting by feeding back information about previously reported reactions and numbers and origin of reports in a more frequent and informative manner:

P12: "If you saw some examples of things people had reported and outcomes, if there was a positive outcome of it then I think that would encourage you to report them, you'd know the benefits of reporting."

P17 "I certainly would be interested in what comes out of our hospital and what proportion of it is from pharmacists. That information is probably not as readily available as I'd like it to be. I'd be interested what the national figures were so you could benchmark yourself against that and hope to increase it."

6.4.2 Regional Monitoring Centres.

Pharmacists' opinions of the local CSM / MCA RMC varied depending on their proximity with the unit and the nature of previous contact, if any. Those who had used the unit had found it be useful and that knowing the staff on a personal basis and its local situation, encouraged them to use it. Those who had not used the RMC were largely ambivalent about its purpose and presence. Pharmacists appeared to be unclear as to the exact role of the RMCs:

P34: "I don't really know what sort of role they fulfil at all. I think perhaps they should be giving more of the education that we need. To be honest I didn't even know there was one."

6.4.3 The Black Triangle Intensive Monitoring Scheme.

Pharmacists were knowledgeable and largely positive about the benefits of the black triangle scheme. The fact that any suspected reaction should be reported removed many of the concerns about whether a report should be made.

Reporting of minor reactions to black triangle drugs. Pharmacists had mixed views about whether a drug's status in terms of the black triangle, would encourage them to report minor or less important reactions; 14 (36.8%) said

they would, 10 (26.3%) said they would not and the remainder said that it would depend on the circumstances at the time of the reaction. Whether a reaction was listed in the product's Data Sheet or Summary of Product Characteristics appeared to be an important factor in deciding whether to report:

P25: "It depends on what kind of drug it was, if it was a completely new chemical entity yes I would."

6.4.4 Criteria for reporting.

Pharmacists had mixed opinions about the criteria for reporting ADRs. Pharmacists who had participated in education and training sessions appeared to be either more knowledgeable or less concerned about the criteria for reporting ADRs whereas other pharmacists, particularly those newly qualified, expressed concerns about reporting inappropriately.

P12: "I'm not sure when to report and when not to so I end up being overcautious really, you know, because you don't want to just start sending in a form for everything so..."

P10: "I think the criteria are pretty good actually. I think its easier in a hospital situation knowing more accurately what to report because of things like, what extends hospital stay or what causes admission. I suppose, if you're not seeing patients from that situation, then things might be harder to fit into the criteria."

P11: "It's perhaps not clear to other pharmacists or even clinicians who've not had additional training. They tend to focus on black triangle drugs and don't report well known reactions."

P9: "Well in theory they're okay but once you get down to it its not so easy and there are some cases where it's a bit unclear. What's not serious to the CSM / MCA might well be serious to the poor sod that's got to put up with it! I mean some things that medics think, and we think patients should put up with, aren't really all that pleasant and it's easy to overlook that. I probably use my own interpretation of what the criteria are if I'm honest."

P1: "Because I'm newly qualified I would seek advice from other members of the department. If they were of the opinion that it wasn't worth reporting then I probably wouldn't - I'd listen to them."

6.4.5 Comments on the Yellow Card.

Pharmacists were generally satisfied with the layout and required content of the Yellow Card. Lack of space for additional medication was the only problem identified on a number of occasions although some pharmacists correctly identified the option to put this information on the back of the card or on an additional sheet. Pharmacists were generally unconcerned by the use of a separate reporting card for pharmacists. Many thought it appropriate because the CSM / MCA would want to compare pharmacists' reports with other professions and to audit the implementation of the scheme. Some pharmacists did not approve of the use of separate cards and the fact that Yellow Cards

were not available in the BNF was also highlighted. As a result, a minority of pharmacists felt their participation in the Yellow Card Scheme was not fully supported by the CSM / MCA and that they were perceived as "second class" reporters.

6.4.6 Participation in the scheme to date.

Of those interviewed, 15 (39.5%) had not reported an ADR via the Yellow Card Scheme, 7 (18.4%) had reported a single ADR, 12 (31.5%) had reported between two and four reports and only 4 (10.5%) had reported 5 or more ADRs. Pharmacists had reported a mean of 1.8 Yellow Cards (± 2.1, range 0-8). Most pharmacists commented that their contribution had been somewhat less than it could have been. Many pharmacists who had reported one or two Yellow Card reports had done so shortly after the scheme had been launched and had not reported once the 'novelty' had worn off:

P3: "I did one early on, just after it started, I think I made more of an effort because we had just been allowed to report."

P21: "I think there's probably more that I've missed but I think pressure of work ...I've either not picked them up or not reported them."

There was no real consensus as to why pharmacists had reported some reactions and not others suggesting that the decision is often made either on a whim or depending on the circumstances that pharmacists find themselves in at

the time. Many were stimulated to report by reactions that had been to a black triangle drug, had resulted in hospital admission or had been particularly serious. Others had reported less notable reactions that complied with the CSM / MCA criteria or reported because doctors had been unwilling to do so:

P20: "Probably the severity. The one I remember clearly was a child who ended up on intensive care with Steven's Johnson Syndrome....."

P30: "The one where a patient was accidentally re-challenged with the drug and had the same reaction - I felt very definite about that, it was very.... worth reporting."

6.4.7 Relations with medical staff.

Overall, the fact that doctors receive a copy of their ADR report did not concern pharmacists. Most stated that they would not report an ADR without either informing the patient's doctor or discussing it with them first to obtain a second opinion:

P10: "I work in a team anyway so I'm quite happy for the doctor to know. In fact I'd probably mention that I was filling a form in."

P15: "Well I always generally discuss it with them anyway, if only to get their feeling as to whether it was or not."

However, many pharmacists were concerned about reporting ADRs in situations where they disagreed with the patient's doctor about whether an ADR had

occurred or should be reported via a Yellow Card. One suggestion was that the option to report in confidence should be included in the reporting protocol:

P9: "I think if there's disagreement you should be allowed, as a healthcare professional to make up your own mind and to be able to report something without having to get permission."

6.4.8 Causality of reactions.

Pharmacists had some concerns over the certainty that a reaction had occurred and some would be deterred from reporting reactions that were unlikely or somewhat bizarre. Many suggested that they would contact the patient's doctor or discuss it with colleagues to obtain a second opinion before reporting. Some pharmacists were also conscious of the CSM / MCA's concerns about inappropriate reports and were reluctant to report potentially implausible reactions:

P28: "People aren't prepared to report unless they're 90% certain it is a reaction. I think we should be encouraging reporting between 50% and 90%, that sort of area because I'm sure a lot don't get reported. That's where we come in really...."

P18: "Probably I'd consult with the doctor and see what their opinions were. It could be something clinical that you don't actually know about that patient. But if they can't really establish why its happening, yes, I'd probably report."

P30: "I'd have to pretty certain about something before I reported it. You'd have to be fairly sure it was a reaction to that drug but if it was a black triangle drug I'd probably report with a note saying this seems a bit strange to me but for all I know there could be ten more people sending in the same reaction, I mean every reaction's a little unusual the first time it happens."

Several pharmacists commented that ADRs were identified by chance rather than by a deliberate approach:

P17: "There are an awful lot of things that we have to do when we go out onto wards and therefore its a bit serendipitous if we pick them up. I would say a lot of the ones we do report, are the ones that are reported to us. Sometimes patients will mention something or sometimes someone will say, "do you think this is a side effect?""

P37: "I don't think they're pointed out for us, I think its more something you tend to spot. I mean I would look at, if something's crossed off for no obvious reason, I'd look at that and I'd find out why. Or, if someone's prescribed calamine or chlorpheniramine, look and see if they had a rash from a drug or something.... more often than not, if something's been stopped suddenly."

6.4.9 Motivation in reporting.

Most pharmacists stated that they felt motivated to report ADRs in principle although as demonstrated by their participation in the scheme, practice did not reflect this. Others were less enthusiastic about the scheme:

P13: "I don't feel demotivated, so by inference, I suppose I am motivated. I just need to think about it."

P16: "I'd like to think I'm committed to it. You know, when the opportunity arises I would feel motivated to do something about it. I don't think it's something we should turn our back on."

P23: "ADRs is not something I feel terribly motivated towards, which I do recognise is a bad thing because they do need to be reported."

6.4.10 Patient confidentiality.

Pharmacists were unconcerned about reporting patient details in terms of confidentiality. They were generally aware that information from Yellow Cards was treated in confidence and that they could report without identifying the patient, if required.

6.4.11 Attitudes towards hospital pharmacists' role in reporting via the Yellow Card Scheme.

In response to their submission of a Yellow Card, pharmacists were generally unconcerned regarding the nature of feedback provided by the CSM / MCA and most stated that an acknowledgement letter or quantification of previous reports would suffice. One paediatric pharmacist commented that the data were of limited use as it was not categorised by age. Most were satisfied with the current provision of information, that is, details of numbers of previous reports, with few requiring further information. Pharmacists were concerned about the

quality of their report with many suggesting that it would be beneficial for them to be provided with feedback on the quality of their report. However, some expressed concern that individual feedback about inappropriate reports would dissuade people from reporting again and suggested the use of generic feedback:

P27: "Certainly if they though my report was rubbish I'd want to know and I'd use that positively. If you don't, then you're going to carry on reporting rubbish in blissful ignorance for ever more."

A few pharmacists expressed the opinion that using the information that the CSM / MCA provides via drug analysis prints and individual case reports placed a responsibility to the user to contribute to that database or illustrated the problems associated with underreporting. Some commented that they used this data in their day to day practice:

P3: "It's not till you use the data, you know , you've got it on the screen that you think perhaps I should do more. You think at the end of the day, it doesn't mean a lot when you put it into context, its only out of so many that haven't been reported ."

When asked about Current Problems in Pharmacovigilance, nearly all pharmacists were enthusiastic about its content and format. Most pharmacists said they read it and that the brief and informative manner in which items were presented encouraged them to read it. Many commented that they used the information in practice:

P11: "I think I've used it in arguments, well not arguments, more discussions really with clinicians to back yourself up, for example the recent one with cisapride, we were discussing that just recently on a ward round. It sort of backs up your argument, that is, if the CSM / MCA are worried, then we should be too."

6.4.12 Reasons for under-reporting.

Pharmacists were reluctant to report well known reactions despite their awareness of the need to do so:

P4: "If you saw something serious then you might think, lets get something filled in here, whereas, if its something that you know is regularly reported on, then you might not."

Many pharmacists quoted pressure of work as the reason for their lack of participation in the scheme. Most stated that it was a lack of time preventing them from identifyng ADRs in practice that was the problem rather than the time required to complete a Yellow Card:

P2: "Its something that's taken a back seat because of the circumstances in our department. There's a limited number of staff within the system and other priorities have taken the lead."

P3: "You might see an ADR but you come back from the wards and you get thrown into something straight away and once you've left it, then it never gets done."

Some pharmacists stated that they had yet to accept it as part of their everyday practice and that it was not one of their main priorities:

P23: "....when I look at the things I need to do in one day its not something that's very high on my list."

Some pharmacists were concerned by their lack of clinical knowledge and felt that this was an area where doctors could assist them:

P16: "We're not doctors and I think some of my colleagues forget that sometimes. My diagnostic skills are male, female, bald, young, fat, thin and that's it. If I wasn't sure I'd seek some help or confirmation from the doctor."

P15: "Yes, it sometimes bothers me that I might not have a total grasp of the condition the patients have but on the other hand, I know I can do a better job when it comes to drug details so I don't know...it's a bit of a balance really."

6.4.13 Education and training.

Training was identified as an issue that would increase reporting and awareness of ADRs. Pharmacists who had been on the CSM / MCA RMC study day found the course beneficial. A deeper understanding of the Yellow Card Scheme and its purpose and intricacies appeared to motivate pharmacists either to report or

to be more concerned with participating in the scheme and its importance. Many stated that they had attended educational sessions as a pre-registration trainee or as a diploma student but that little had happened since then:

P28: "Yes when we were first able to report we did a lunchtime seminar on ADRs and encouraging pharmacists to report and what we could do and also trying to get doctors to report. But that was a one off event really."

P11: "Certainly the study day made me more aware and more likely to report. Unfortunately I'm the only one from our department who's been and as far as I know, they've not run another one and I think maybe if we got more pharmacists on that, that would help."

Pharmacists suggested that departments could encourage them to report ADRs by increasing time on the wards, development of a local scheme and by raising it as an issue within the department via departmental meetings:

P24: "After we had a talk you were more aware of them, but that was a year and a half ago and we've not had anything since and perhaps we should do more regularly. It possibly needs other sessions or a six monthly review to see what people are reporting and how many just to keep people aware of what's going on."

6.4.14 The concept of a fee.

All pharmacists were generally opposed to the concept and a number expressed concern about inappropriate reporting. Although some stated that financial reward would be most welcome, many were concerned that reporting ADRs was a professional issue and should not be financially driven:

P16: "A fee? Well I suppose it would stimulate some interest. It would be disappointing that we were needed to be paid to do something like that."

6.4.15 Local schemes.

Pharmacists involved in local schemes stated that they found they were encouraged to report ADRs. Local schemes were useful for collating data within a hospital and for ward staff to communicate reports via official channels. Schemes were also described as sifting mechanisms for ADR reports from a quality control aspect. Some pharmacists in hospitals without schemes expressed a desire for their hospital to initiate one.

6.4.16 Pharmaceutical companies.

Pharmacists felt that drug companies were helpful in dealing with their ADR related queries and many commented that they were far more prompt than the CSM / MCA in providing written information. Although many were aware that it was a legal requirement, almost all pharmacists felt antagonised by the requests for further information from drug companies.

6.4.17 Professional responsibility.

Pharmacists generally agreed that reporting was a professional responsibility and felt that it was an important part of their role:

P13: "You're involved in the safe, effective and economic use of drugs. A part of that is the possibility that it might cause adverse effects and you've got to manage that. Reporting should be expected, it should be the norm."

6.4.18 Attitudes towards the introduction of reporting for hospital pharmacists.

The introduction of direct reporting for pharmacists. The introduction of reporting for pharmacists was seen as a positive development by the majority of those interviewed. Many felt it was appropriate considering pharmacists' knowledge of drugs. In some cases, pharmacists had been involved in reporting ADRs either as part of a local scheme, assisting doctors to complete reports or merely obtaining a doctor's signature prior to submitting reports themselves. It was widely felt that reporting for pharmacists should have been introduced much earlier. The role of the Royal Pharmaceutical Society of Great Britain was perceived to have been disappointing in the introduction and subsequent promotion of the scheme:

P16: " I think they're (the RPSGB) very lax in their approach to developing a proper professional approach... but they've taken too much of a back seat on it.

Things like this that we should embrace, maybe they've not done and provided as much support as there should have been."

6.4.19 The processes involved in the introduction of reporting.

Pharmacists were generally dissatisfied with the process of the introduction of reporting. Many felt that there had been little publicity about the development and a number of pharmacists also commented that there had been little follow up after the introduction of reporting:

P14: "....it just sort of came in. Everyone was sent booklets about it but there wasn't a huge amount of fanfare about it."

P17: "....there seemed to be little consultation, one minute we couldn't and the next minute we could. Maybe I missed a lot of the pre-press about it, it seemed to suddenly happen rather than evolve."

Conversely, a minority of pharmacists was satisfied with the level of information provided:

P 15: "It was well publicised and I think the material that we got was sufficient for us to get on with it."

6.4.20 CSM / MCA Information Pack.

The information pack designed to support the launch of pharmacist reporting was well received by pharmacists. Many had retained the pack as an information resource and used in as a training resource:

P28: "I thought it was quite basic but I wasn't sure we needed anything else quite frankly. I think it illustrates what you should report and what you shouldn't, I felt I knew most of it quite honestly but there again I thought it was a good reminder to everybody."

Approximately half of those interviewed considered themselves ill-prepared to participate in the scheme when it was introduced. Some seemed prepared to 'have a go' while others were reluctant to report when they were unsure of exactly what was required. Some stated that their previous involvement in the completion of reports had prepared them for this role.

6.4.21 Final thoughts - viewpoints.

Pharmacists were asked to give their final thoughts or observations on the scheme. Most felt that promotion of the scheme was important to encourage pharmacists to participate:

P17: "Well I hope it continues and I hope we continue to build up our role in it as the level of reporting that's coming out so far is pretty discouraging, I was under the impression that we weren't doing too badly but I know we could certainly do a lot better...."

P18: "I think it is everyone's responsibility. You can't say its just pharmacists, it needs input from everybody."

P19: "Pharmacists don't seem to have taken up the challenge of showing that they are an important source of spotting ADRs. Possibly they're not in the right place at the right time, they're not as involved with the patient enough."

P25: "I think its something that will grow into practice. It should be built into pre-reg. training, basic grade training and even diploma training. It will be interesting to see what the quality and amount of reporting is like in a few years time."

6.5 Discussion.

Despite the campaign for ADR reporting for pharmacists continuing for over ten years,[32] it was considered that its introduction was precipitous and that since then, it had been poorly publicised and promoted. Since its introduction, hospital pharmacists' participation in the scheme appears to have been somewhat sporadic. However, it is worth noting that the initial level of doctors' participation in the Yellow Card Scheme was also somewhat slow to reach the level of reporting that exists today.[87] The CSM / MCA generally has a poor image with hospital pharmacists in terms of its accessibility and perceived opinion of pharmacists' role in reporting. However, feedback by the CSM / MCA on individual reports was generally thought of as satisfactory and the Current Problems in Pharmacovigilance publication was highly regarded.

Only 42% of those interviewed had submitted more than a single Yellow Card report and a similar percentage had reported none at all. Whilst hospital pharmacists acknowledge ADR reporting as part of their professional role, it is not yet considered as part of their daily practice. A number of factors appear to be dissuading pharmacists from participating in the scheme. These include clinical factors such as uncertainty about the significance of a reaction and a lack of clinical knowledge. Collaborative reporting, combining doctors' clinical knowledge and pharmacists' pharmaceutical expertise should provide an ideal basis for quality ADR reporting. Pressure of work was also quoted as a deterrent to reporting; a factor that has not been helped by current recruitment difficulties.[74] These difficulties may have been a contributory factor as to why departments have done little to promote reporting and why ADR reporting does not rank as a high priority. Initial schemes for education and training were perceived as having been successful, however, eighteen months after the introduction of reporting, on-going training needs had not been fully addressed either by the CSM / MCA, their RMCs, the RPSGB or by individual hospital pharmacy departments.

Hospital pharmacists did not consider that receiving a fee would increase reporting, in contrast to the opinions of community pharmacists.[11] This issue has been addressed previously by a CSM / MCA working party which concluded that the concept of having a sizeable fee might encourage reporting of trivial reactions while a small fee would not be a spur to reporting.[88] The layout of Yellow Card reporting forms was deemed satisfactory and the concept of a separate card for pharmacists was acceptable. Availability of Yellow Cards was sometimes a problem, which could be overcome by the inclusion in the BNF of

an all purpose Yellow Card rather than one for use by doctors and dentists alone. The role of pharmaceutical companies should be addressed in pharmacovigilance as the negative views expressed by pharmacists about the nature and extent of follow up by company based medical information centres are in some cases deterring pharmacists from utilising a potentially important information source. However, pharmaceutical companies are currently legally obliged to follow up reports of ADRs with the reporting healthcare professional.

6.6 Limitations of this study.

The sample was restricted to main hospitals within the CSM / MCA Mersey Region. Potentially, there may have been differences in the responses received from hospital pharmacists in smaller hospitals. As interviews were conducted with only 38 of an estimated 200 hospital pharmacists employed in the CSM Mersey catchment area, caution should be exercised in the extrapolation of results to the rest of the population. However, this phase of the study is the first to collect qualitative data about ADR reporting by hospital pharmacists and has provided some insight into the processes affecting their participation in the Yellow Card Scheme.

Chapter 7:

Attitudes of hospital pharmacists to adverse drug reaction reporting and knowledge of the Yellow Card Scheme.

Chapter 7: Attitudes of hospital pharmacists to adverse drug reaction reporting and knowledge of the Yellow Card Scheme.

7.1 Introduction

The previous chapter describes the qualitative approach used to identify pharmacists' attitudes to ADR reporting. This chapter describes a quantitative survey in which the attitudes and knowledge of hospital pharmacists to the Yellow Card Scheme are assessed using quantitative methods and compared with previous studies examining the views of medical practitioners.[20,21]

7.2 Aim

The aim of this component of the study was to investigate the attitudes of hospital pharmacists to ADR reporting and their understanding and knowledge of the Yellow Card Scheme.

7.3 Method

On annual registration with the Royal Pharmaceutical Society of Great Britain (RPSGB), pharmacists are asked to indicate the branch of the profession in which they practice. From the RPSGB computer database, in which approximately 7000 hospital pharmacists are listed, 600 were randomly selected. These pharmacists were sent a postal questionnaire, a covering letter and a prepaid envelope with which to return the completed questionnaire. Four weeks later, a second mailing of the questionnaire was distributed to all 600 pharmacists to encourage non-respondents to participate in the study.

The questionnaire was similar to that used in previous studies examining the attitudes of medical practitioners to ADR reporting.[20,21] The previous qualitative study was also used to formulate the questionnaire (Appendix 4).[89] Pharmacists' knowledge of the Yellow Card Scheme, attitudes to reporting, reasons why they may not report ADRs and concerns about this new role were included in the questionnaire. A list of hypothetical ADRs was included and pharmacists were asked to indicate whether or not they would report them, a method similar to that used by Bateman et al.[21] The number of hypothetical reports for which pharmacists would report / not report in agreement with CSM / MCA criteria was recorded; a method reported by other workers.[90] A senior member of the CSM / MCA reviewed the questionnaire prior to its distribution and comments and suggestions were incorporated into the questionnaire.

The questionnaire was piloted on 20 randomly selected hospital pharmacists of whom 12 (60%) responded. A follow up mailing was not distributed. One question was identified as ambiguous and altered accordingly. The` pilot study also identified one retired pharmacist and one not in hospital practice. Enquiries to the RPSGB revealed that the database did include pharmacists not actively involved in hospital practice and those who had retired. The sample size selected initially was 500, but was increased to 600 to allow for such pharmacists.

Data from this survey were compared with studies performed by Belton et al[20] and Bateman *et al*.[21] Responses in the survey by Bateman *et al* were categorised into six sub-groups of medical practitioners. For the purposes of this study and to simplify comparisons, these categories were merged and re-

calculated as a single numerical value and percentage of the total number of respondents.

Data were analysed using the Statistical Package for Social Sciences (SPSS for MS Windows version 9). Data are presented as mean ± standard deviation (where appropriate) and statistical analysis was performed by chi-squared tests, linear and logistic regression, accepting $p \leq 0.05$ as significant. In all logistic and linear regressions, non-significant predictors ($p > 0.05$) were removed one at a time, until only significant predictors ($p \leq 0.05$) remained.

Factors influencing respondents to report the 6 hypothetical cases in accordance with CSM / MCA criteria were assessed using logistic regression. Three predictors were used, that is, whether a new drug was involved, whether the reaction was not well recognised and whether the reaction was serious. A decision to report or not report each individual reaction (regardless of concordance with CSM / MCA criteria) was used as the dependent variable.

Factors influencing respondents to have participated in the Yellow Card Scheme were also assessed using logistic regression. Five predictors were used, that is, age, length of time in hospital practice, previous education and training, whether pharmacists practised in a CSM / MCA RMC and whether pharmacists considered themselves well informed about the Yellow Card Scheme when it was launched. Whether pharmacists had reported via the Yellow Card Scheme or not, was used as the dependent variable.

Factors influencing pharmacists to comply with CSM / MCA criteria were assessed using linear regression. Four predictors were used, that is, age, length of time in hospital practice, previous education and training and whether pharmacists had ever reported an ADR via the Yellow Card Scheme. The total number of reports that pharmacists would or would not report in accordance with CSM / MCA criteria was used as the dependent variable.

7.4 Results.

7.4.1 Demographics.

Following distribution of 600 questionnaires, 322 (53.7%) were returned. Seventeen respondents (2.6%) stated that they were retired or no longer practising as hospital pharmacists, and were thus excluded. The age of the remaining respondents (n=305) ranged from 22 - 65 years (mean 36.1 ± 9.1 years) and number of years qualified ranged from 1 - 42 years (mean 13.7 ± 9.1 years). Respondents' time in hospital practice ranged from 1 - 34 years (mean 11.2 ± 7.1 years). Of those surveyed, 85 (27.8%) practised in an area covered by one of the CSM / MCA RMCs, 109 (35.7%) were not in a RMC, and 106 (35.1%) stated they did not know (4 (1.3%) did not respond).

7.4.2 The Yellow Card Scheme and pharmacovigilance.

Of those surveyed, 296 (97.0%) knew that they were allowed to report ADRs via the Yellow Card Scheme. Of these, 224 (75.7%) knew about the scheme from reports in the Pharmaceutical Journal, 117 (39.5%) via departmental meetings or announcements, 113 (38.2%) through discussion with colleagues and 153

(51.7%) had received a copy of the CSM / MCA Information Pack. A small number of pharmacists (frequency less than 10 in each case) stated that they had heard about the scheme through the Centre for Pharmacy Postgraduate Education (CPPE) scheme, postgraduate education courses, drug information training days and pre-registration training. Of those surveyed, 172 (56.0%) considered that they had been adequately informed about the launch of the scheme, while 72 (23.6%) did not, and 60 (19.7%) could not remember. A Yellow Card report had been submitted to the CSM / MCA by 78 (25.6%) of those responding. Overall (that is, reporters and non-reporters), the 305 pharmacists returning questionnaires had reported a total of 217 Yellow Cards (mean per pharmacist 0.7 ± 2.4 Yellow Cards, range 0 - 30). Pharmacists that had reported ADRs had submitted a mean of 2.8 ± 4.2 Yellow Cards.

Pharmacists were asked, using an open question, to explain what they understood by an inverted black triangle▼ placed next to a medicine. Responses varied with 171 (56.1%) pharmacists stating that it was a new drug and that all reactions should be reported, while 97 (31.8%) stated that it was either a new drug or stated that all reactions should be reported. The remainder either did not answer (n=25 (8.2%)) or did not know (n=12 (3.9%)). Asked whether the CSM / MCA wished to receive 'only proven ADRs', 284 (94.0%) correctly stated this was false, only 2 (0.7%) stated this was true and 16 (5.3%) did not know. Pharmacists were also asked to identify the nature of reports the CSM / MCA wished to receive for specific groups of drugs (Table 7.1). In comparison to medical practitioners surveyed by Belton *et al.*[20] and Bateman *et al* [21], answers were similar between the groups. However, pharmacists were less aware of the criteria for reporting vaccines than doctors in the Bateman *et*

al study.[21] but comparable to those surveyed by Belton *et al.*[20] The reasons for this discrepancy are unclear.

Table 7.1: Appropriateness for CSM / MCA reports

Category (correct response)	All reactions	Serious reactions	No reactions	Don't Know	Bateman et al[1] (n=1181)	Belton et al[1] (n=261)
Newly marketed agents▼ (all reactions) (n=305)	97.7% (298)	0.7% (2)	0.0% (0)	1.6% (5)	93.1% (1100) p<0.003	97 %[2] (253) [3% were not sure]
Established products (serious reactions) (n=304)	6.6% (20)	91.4% (278)	0.7% (2)	1.3% (4)	93.7% (1107)	95%[3] (248) [3% were not sure]
Vaccines (all reactions) (n=304)	56.3% (171)	23.0% (70)	0.7% (2)	20.1% (61)	77.2% (912) p<0.0001	59% (155) [26% were not sure]
Herbal drugs (all reactions) (n=304)	36.2% (110)	15.8% (48)	4.6% (14)	43.4% (132)	N/A	NA

1. Percentage and number answering statement correctly
2. 6% agreed with statement "Only serious reactions to new products"; 7% were not sure.
3. 47% agreed with "All suspected reactions to established products", 19% were not sure.

Rounding up means percentages are greater than 100%

N.B. P values were calculated using χ^2 tests comparing responses from either Bateman *et al* or Belton *et al* with pharmacists' responses

Pharmacists were asked to identify the purpose of the Yellow Card Scheme from 6 statements (Table 7.2). Pharmacists generally knew the purpose of the scheme but many incorrectly thought that the scheme could be used to calculate the incidence of ADRs and that safe drugs could be identified through the scheme. In comparison to the surveys of medical practitioners,[20,21] pharmacists were less aware of the real purposes of the scheme and significant differences existed in answer to four of the questions posed.

Table 7.2: Purpose of the Yellow Card Scheme

Question (Correct response)	Yes	No	Don't Know	Bateman et al[1] (n=1181)	Belton et al[1] (n=250)
To enable safe drugs to be identified (No)[2] (n=298)	41.0% (122)	46.0% (137)	13.1% (39)	33.8% (400) p<0.0001	21% (52) [15% not sure] p<0.0001
To measure the incidence of ADRs (No) (n=302)	82.5% (249)	14.2% (43)	3.3% (10)	56.9% (872) p<0.0001	22% (56) [10% not sure] p=0.01
To identify factors predisposing patients to ADRs (Yes) (n=302)	75.2% (227)	10.6% (32)	14.2% (43)	84.2% (994) p=0.0003	73% (183) [21% not sure]
To identify previously unrecognised ADRs (Yes)[2] (n=305)	98.0% (299)	0.3% (1)	1.6% (5)	99.2% (1171)	98% (244) [2% not sure]
To obtain information about the characteristics of reactions (Yes) (n=301)	62.5% (188)	17.9% (54)	19.6% (59)	NA	71% (178) [22% not sure] p=0.03
To compare the adverse effects of drugs in the same therapeutic class (Yes) (n=304)	65.1% (198)	19.4% (59)	15.5% (47)	59.9% (707)	NA

1. Number and percentage answering correctly
2. Rounding up means percentages may not equal 100%

N.B. P values were calculated using χ^2 tests comparing responses from either Bateman *et al* or Belton *et al* with pharmacists' responses

7.4.3 Attitudes to reporting.

Pharmacists were asked to state whether they agreed or disagreed with the statements about ADR reporting (Table 7.3).

Table 7.3: Attitudes to ADR reporting[3]

Statement	Agree	Disagree	No opinion	Bateman et al[1] (n=1181)
ADR reporting is a professional obligation for pharmacists (n=302)	86.1% (260)	5.0% (15)	8.9% (27)	94.8% (1119) p<0.0001
One ADR report makes no difference to the Yellow Card Scheme (n=303)	2.0% (6)	94.7% (287)	3.3% (10)	15.5% (183) p<0.0001
All serious ADRs are identified by the time a drug is marketed (n=304)	0.0% (0)	98.4% (299)	1.6% (5)	19.1% (226) p<0.0001
Yellow Cards are too complicated to fill in n=304)	9.5% (29)	72.7% (221)	17.8% (54)	50.6%[2] (598) p<0.0001
It is adequately clear to me what I should and should not report to the CSM / MCA (n=300)	56.0% (168)	34.0% (102)	10.0% (30)	NA

1. Percentage and number agreeing with statement
2. 'Would report if there was an easier method'
3. Did not feature in survey by Belton et al

N.B. P values were calculated using χ^2 tests comparing responses from Bateman *et al* with pharmacists' responses

While over half of the doctors surveyed by Bateman *et al*[21] felt that Yellow Cards were too complicated to fill in, only a tenth of pharmacists agreed with this statement. Significantly fewer pharmacists thought that "one Yellow Card made no difference to the scheme" and none thought that "all serious ADRs are identified by the time a drug is marketed". When asked whether ADR reporting should be compulsory, 152 (49.8%) stated that it should (despite the fact that only a quarter had reported), 131 (43.0%) stated that it should be voluntary, and 22 (7.1%) were either unsure or did not respond. There was no significant difference between reporters and non-reporters opinions as to whether reporting should be compulsory or voluntary (χ^2= 1.5, p=0.5).

7.4.4 Pharmaceutical Manufacturers.

Of those surveyed, 260 (85.2%) had, on at least one occasion, contacted a pharmaceutical manufacturer for information concerning a suspected ADR. Of these, 248 (95.4%) had been sent forms or documents from the pharmaceutical company to be completed as a result of their enquiry. Sixty seven (27.0%) stated that these requests would deter them from contacting companies in future.

7.4.5 Reporting ADRs.

Pharmacists were asked what would influence them in deciding whether to report an ADR (Table 7.4). High proportions of pharmacists and medical practitioners [20,21,90] would be encouraged to report serious or unusual reactions or those related to new products although the proportion of pharmacists quoting these reasons was significantly higher than the medical practitioners. However,

the largest difference was that over four fifths of pharmacists would be encouraged to report an ADR if they were certain a reaction had occurred in comparison to half of those surveyed by Bateman *et al*.[21]

Table 7.4: Factors encouraging pharmacists to report an ADR

Factor	Agree	Disagree	Bateman et al[1] (n=1181)	Belton et al[1,2] (n=261)
The reaction is of a serious nature (n=280)	99.3% (278)	0.7% (2)	80.2%[2] (947) p<0.0001	95% (247) [2% not sure] p=0.001
The reaction is unusual (n=280)	98.6% (276)	1.4% (4)	95.0%[3] (1122) p<0.008	89% (232) [9% not sure] p<0.0001
The reaction is to a new product (n=280)	99.3% (278)	0.7% (2)	90.4% (1068) p<0.0001	91% (237) [7% not sure] p<0.0001
Certainty that the reaction is true ADR (n=278)	82.4% (229)	17.6% (49)	NA	49% (129) [31% not sure] p<0.0001
The reaction is well recognised for a particular agent (n=276)	12.7% (35)	87.3% (241)	60.0% (709) p<0.0001	NA

1. Number and percentage agreeing with statement
2. Respondents asked to state 'Important' / 'Unimportant' / 'Not sure'
3. Respondents asked if 'Severity' is an important factor in deciding to send in a Yellow Card.

N.B. P values were calculated using χ^2 tests comparing responses from either Bateman *et al* or Belton *et al* with pharmacists' responses

Over a third of those surveyed had, at some time, either not reported an ADR knowing that a doctor was going to report it (107 (37.2%)), or had completed a

Yellow Card for a doctor to sign (65 (22.6%)). Of those surveyed, 126 (43.8%) had access to CSM / MCA information in either microfiche or CD-ROM format in their department, while 48 (16.7%) did not know. CSM / MCA data had been used by 200 (69.4%) pharmacists in their evaluation of potential ADRs. Of those responding, only 125 (43.4%) knew that patients' doctors or consultants received a copy of their report from the CSM / MCA.

Pharmacists were asked to state the factors that might discourage them from reporting ADRs (Table 7.5). Significant differences existed between professions in terms of deterrents to reporting. Of those surveyed by Belton *et al*,[20] significantly fewer were deterred from reporting by a lack of time or concern about submitting an inappropriate report although more were deterred by a lack of report forms. In comparison to those surveyed by Bateman *et al*,[21] pharmacists were significantly more likely to be deterred by a lack of time but less concerned by the absence of a fee or concern that reporting would generate extra work.

Table 7.5: Reasons for not reporting ADRs

Reason	Agree	Disagree	Bateman et al[1] (n=1181)	Belton et al[1,3] (n=260)
Concern that a doctor gets a copy of my Yellow Card (n=279)	9.0% (25)	91.0% (254)	NA	NA
Lack of confidence in discussing the ADR with the prescriber (n=278)	16.2% (45)	83.8% (233)	NA	NA
Apprehension about sending in an inappropriate report (n=279)	33.7% (94)	66.3% (185)	NA	8%[4] (20) [10% were not sure] p<0.0001
Lack of time to fill in a report (n=279)	45.2% (126)	54.8% (153)	27.7% (327) p=0.005	21% (54) [17% were not sure] p<0.0001
Concern that a report will generate extra work (n=279)	17.6% (49)	82.4% (230)	29.3%[2] (346) p<0.0001	NA
The absence of a fee for reporting ADRs (n=279)	5.0% (14)	95.0% (265)	15.0% (177) p<0.0001	NA
Lack of time to actively look for ADRs while in clinical practice (n=278)	56.8% (158)	43.2% (120)	NA	NA
Level of clinical knowledge makes it difficult to decide whether or not an ADR has occurred (n=279)	32.3% (90)	67.7% (189)	NA	NA
Don't feel the need to report well recognised reactions (n=279)	40.9% (114)	59.1% (165)	NA	NA
Pharmacists Yellow Cards not available when needed (n=279)	9.7% (27)	90.3% (252)	NA	21%[5] (55) [5% were not sure] p=0.0002

1. Number and percentage agreeing with statement
2. Reporting results in 'badgering by the CSM
3. Responses were 'Yes' / 'No' / 'Not Sure'
4. Actual question "Doctor fears he / she may appear foolish about reporting a suspected reaction".
5. Actual question referred to "report forms"

N.B. P values were calculated using χ^2 tests comparing responses from either Bateman *et al* or Belton *et al* with pharmacists' responses

Pharmacists were provided with a list of hypothetical ADRs and asked to state which ones they would report to the CSM / MCA (Table 7.6).

Table 7.6: Reporting reactions

Reaction	Agree	Disagree	Don't know
Jaundice with frusemide (n=273)	72.5% (198)	12.5% (34)	15.0% (41)
Headache with venlafaxine▼ (n=271)	47.6% (129)	38.4% (104)	14.0% (38)
Cold extremities with B-blockers (n=276)	0.4% (1)	96.0% (265)	3.6% (10)
Thrombocytopenia with heparin (n=277)	41.5% (115)	49.8% (138)	8.7% (24)
Nausea with montelukast▼ (n=274)	70.1% (192)	18.6% (51)	11.3% (31)
Gastrointestinal bleed with diclofenac (n=278)	33.1% (92)	60.8% (169)	6.1% (17)

▼Symbols were not included in the questionnaire

Of the five examples that were (applying the CSM / MCA criteria) appropriate for a Yellow Card report, pharmacists would, overall, report a mean of 3.7 (± 1.7) ADRs. Significantly fewer would report headache with venlafaxine than nausea with montelukast ($p<0.001$) and significantly fewer would report thrombocytopenia with heparin and a gastrointestinal bleed with diclofenac than jaundice with frusemide ($p<0.001$). A significant difference also existed between the number of respondents that would report the diclofenac and heparin reactions ($p<0.05$).

Pharmacists' scores of appropriately stating they would report reactions in accordance with the CSM / MCA criteria were assessed using linear regression. Pharmacists who had previously reported, and had previously undertaken education and training were found to be significantly and positively associated with participation in the scheme ($p<0.0001$). Logistic regression demonstrated that pharmacists would be significantly more likely to report reactions that were serious, to new drugs or that were not well associated with that drug ($p<0.0001$).

7.4.6 Education and training.

Some form of education and training concerning ADRs had been received by 109 (37.9%) pharmacists. Of those who had received training, 74 (67.9%) had attended departmental meetings, 11 (10.1%) had attended a CSM / MCA study day / evening, 8 (7.3%) had attended formal teaching sessions (pre-registration training and postgraduate education), 5 (4.6%) had undertaken CPPE distance learning packages and 7 (6.4%) had attended training led by drug information pharmacists or centres. Those who had undertaken training were significantly

more likely to have reported an ADR ($p<0.0001$), scored significantly higher on the criteria for reporting ($p=0.001$), would be more likely to report more of the example scenarios ($p<0.0001$) and a trend suggested that they knew more about the purposes of the Yellow Card Scheme ($p=0.07$). Those who considered themselves adequately informed about the launch of Yellow Card reporting for pharmacists were also significantly more likely to have participated in the Yellow Card Scheme ($p<0.001$). Education and training was the only positive predictor identified using logistic regression that influenced pharmacists to report ($p=0.001$).

7.4.7 Increasing reporting.

When asked how ADR reporting could be improved (open question), pharmacists gave a wide variety of responses. The most frequently cited comments included education, training and study days or evenings (62), more time to spend on wards with patients (31), more feedback, reminders and increased awareness (21), encouragement from managers and departments (13), increased collaboration with prescribers and participation on ward rounds (12), increased accessibility of Yellow Cards and cards specifically designed for the use of pharmacists (13) and more publicity in journals about the scheme (8). Other proposals (frequency less than 7) included on-line access or telephone based reporting, development of local initiatives, increased confidence in dealing with medical staff, making reporting a professional responsibility, a fee for reporting, ADR specialist pharmacists and increasing awareness among other professionals that pharmacists could report ADRs.

7.5 Discussion.

7.5.1 Response rate.

The response rate is arguably higher than figures indicate. The number of hospital pharmacists in the UK has been reported at 4500 full time equivalents, thus, the 7000 pharmacists on the RPSGB database is somewhat overstated.[91] It is probable that a significant proportion of those surveyed would not have been eligible for the survey and that not all pharmacists' registered address is their current address. This survey's sample of respondents represents approximately 5% of the hospital pharmacists registered in the UK, a higher proportion than the studies involving medical practitioners used for comparison in this chapter.[20,21]

7.5.2 Knowledge of, and participation in the Yellow Card Scheme.

The aim of this study was, using a postal questionnaire, to evaluate the attitudes and knowledge of hospital pharmacists to the Yellow Card spontaneous ADR reporting scheme. Pharmacists were generally aware of the purposes of the scheme and which ADRs should be reported but lacked knowledge in specific areas. Pharmacists were less aware than their medical colleagues[20,21] of the purpose and usefulness of the information collected by scheme and reasons for this are unclear. This may have important implications as to why the majority of pharmacists in this study would not report the recognised but serious reactions shown in Table 7.6. Paradoxically, the review of the first year of hospital pharmacists' reporting suggested that well recognised but serious reactions constituted the majority of Yellow Card reports that were made in practice.[83] This analysis also showed that overall, they reported a significantly lower

proportion of black triangle drugs than their medical counterparts ($p<0.0001$) but that the proportion of serious reactions reported to these agents was significantly higher ($p=0.01$).[83] Combined with responses obtained from this questionnaire and the qualitative work described in Chapter 6,[89] this suggests that pharmacists are either reluctant to report minor reactions to these agents (also a finding of the previous chapter) or do not perceive the contribution this data can make to post-marketing surveillance as important.

7.5.3 Attitudes to reporting.

With regard to attitudes to ADR reporting, none of the pharmacists thought all serious ADRs were identified by the time a drug is marketed in comparison to the 19.1% in the Bateman *et al* study.[21] This is possibly due to high profile withdrawals of drugs prior to this survey, for example, troglitazone[92] and the reclassification of terfenadine.[16] That significantly less pharmacists thought that Yellow Cards were too complicated to fill in than doctors could reflect cultural differences between professions. It was encouraging that a large majority of those surveyed consider reporting to be a professional obligation and that half thought reporting should be compulsory. Since only a quarter of those responding had reported an ADR, this may have been to add an incentive to report. Over two thirds of pharmacists had used CSM / MCA data in their clinical activities, suggesting that the majority of pharmacists find it of use, despite their failure, or reluctance to contribute to the database itself.

Regarding factors influencing reporting, nearly all pharmacists would be encouraged to report if a reaction was serious, to a new product or an unusual

reaction which was similar to the findings of other studies.[20,21] Paradoxically, over three quarters stated that they would be encouraged to report if they were certain it was a true ADR while previously in the questionnaire, almost all respondents knew that the CSM / MCA did not only want to receive reports of proven reactions.

7.5.4 Factors discouraging reporting.

In terms of factors discouraging pharmacists from reporting, none of the proposed reasons appeared to discourage the majority of pharmacists, with the exception of a lack of time in clinical practice. The proportion selecting this reason and also a lack of time to complete reports was significantly higher than that found in previous work (Table 7.5, $p<0.001$)[20,21,90] and probably reflects different working practices between the professions and current recruitment difficulties within the pharmacy profession.[74] Time was also the most frequently cited factor that would improve pharmacists' involvement in ADR reporting in response to an open question and some felt that departments and managers could help by allowing them more time and encouraging them to participate in this activity. However, whether this would work in practice is debatable, as there are probably many clinical activities for which pharmacists consider themselves to have insufficient time.

A fee was not considered to be an incentive to report. This issue has been addressed previously by a CSM / MCA working party which concluded that the concept of having a sizeable fee might encourage reporting of trivial reactions while a small fee would not be a spur to reporting.[88] Research in an Irish

hospital has shown that the use of a fee can stimulate reporting and that reporting rates drop once the fee has been withdrawn.[22] Pharmacists also stated that participation in ward rounds might aid their identification of ADRs and result in increased reporting of reactions that doctors might not be willing to report. Participation in ward rounds by pharmacists has been shown to result in a decrease in the number of adverse drug events (including ADRs) experienced by patients.[93]

7.5.5 Reporting of examples.

In terms of reporting from the examples of reactions given, three quarters of those responding stated they would report jaundice with frusemide, an unusual and serious reaction, but only half would report thrombocytopenia with heparin and only a third would report a gastrointestinal bleed with diclofenac. This supports the view that most pharmacists would not report well known, albeit serious, reactions but would report unusual ADRs. A disparity was observed in whether pharmacists would report a minor reaction to the black triangle drugs venlafaxine (headache) and montelukast (nausea) and the reason for this is unclear. This difference could be explained by either the longer period venlafaxine has been marketed, or that montelukast is part of a new therapeutic class, or a combination of the two.

Clearly, and despite a good knowledge of the CSM / MCA guidelines for established drugs, pharmacists are somewhat selective in the reactions they consider report-worthy. As stated earlier, analysis of the first year of reporting by hospital pharmacists identified differences in reporting in comparison to their

medical counterparts with regard to new drugs but that the proportion of serious reactions reported for these agents was significantly higher.[83] Combined with responses obtained from this questionnaire, this suggests that pharmacists are either reluctant to report minor reactions to these agents (also a finding of the qualitative work described in Chapter 6) or do not perceive the contribution this data can make to post-marketing surveillance as important. Pharmacists clearly consider that new reactions, ADRs to new drugs and serious reactions as incentives to report.

7.5.6 Education and training.

The findings of this survey demonstrate that education and increased awareness are required to improve pharmacists' knowledge of, and increase participation in the Yellow Card Scheme and to improve their perceptions of the importance of pharmacovigilance, also a finding of other workers regarding Dutch medical practitioners.[90] The infrastructure for the delivery of postgraduate education and training is well established within the pharmacy profession. In particular, the Centre for Postgraduate Pharmacy Education (CPPE) and College of Pharmacy Practice (CPP) have produced and delivered postgraduate education for a number of years, including material relating to ADRs. The role of the RPSGB and the CSM / MCA should also be reviewed in terms of the nature of promotion of the scheme and should perhaps take a more proactive and visible role. It was of some concern that only half of those responding had used the information pack.

Chapter 8:

The development of

HAROLD:

a computer-based system

for the recording and reporting

of adverse drug reactions

reported via a hospital

pharmacy based local

ADR reporting scheme.

Chapter 8: The development of *HAROLD*: a computer-based system for the recording and reporting of adverse drug reactions reported via a hospital pharmacy based local ADR reporting scheme.

8.1 Introduction

A number of articles have been published in the pharmaceutical press concerning the increasing use of information technology for pharmacy - related applications.[62,63,79,94,95,96,97,98,99,100] Activities that were previously cumbersome, repetitive or time consuming may now be completed with significant improvements in efficiency and effectiveness. Computers have an important role in prescribing and dispensing activities, including the detection of drug-drug interactions and drug-disease interactions. Furthermore, computers are involved in monitoring and reporting of pathological tests and are at the forefront of medical information and administrative activities.

This chapter describes the development and introduction of a computer database to record, analyse and report adverse drug reactions (ADRs) at the Royal Liverpool University Hospitals (RLUH).

8.2 Why the database was set up

At the RLUH, audit work within the hospital had revealed that a number of reported ADRs were neither adequately documented in patients' medical records nor communicated to the patients' general practitioners via standard discharge letters or discharge prescription forms.[73] It was therefore decided to introduce an ADR notification programme at the RLUH to ensure that all ADRs

reported via the 'Green Card' scheme were recorded in patients' medical records and that an endorsement of the ADR was made on the cover of patients' medical records. It was also intended to ensure that the details of any ADRs should be passed on to patients' GPs.

Recent advances in the development of the 'Green Card' scheme and an increase in the level of participation of the hospital staff resulted in an increasingly large number of reports being received by the pharmacy each month. As a result, the workload raised by the scheme had risen significantly, placing an increasing encumbrance on the operators of the 'Green Card' scheme. The extra anticipated workload imposed by the new notification program, combined with other pressures, cast doubt upon the feasibility of new system. It was therefore decided to develop a system which could be simple to co-ordinate, utilise minimal time resources and result in an appreciable improvement in current operation of the scheme. As a result, the Hospital Adverse drug Reaction On-Line Database (*HAROLD*) was developed.

8.3 Selection and requirements of the database

A number of database systems have been set up for use in adverse drug reaction monitoring and a number of different programmes have been used. Articles have been published describing the use of Epi-Info, dBASE and Alpha Four in clinical pharmacy activities.[97, 98, 99,100] The database required by the RLUH needed to allow simple, uncomplicated design, simple data entry and automatic generation of reports. The system was also required to be able to

generate reports of a suitable quality for the purposes of communicating data to other healthcare professionals.

The database chosen for use at the RLUH was Microsoft Access (version 2.0). This package was widely available as part of Microsoft Office Professional, which was widely used throughout the United Kingdom and is simple to use once the operator had become familiar with its basic functions. Access could be cross-linked with Microsoft Word (a word processing programme), Microsoft Excel (a spreadsheet / statistical package) and other Microsoft programmes and could automatically generate reports with relative ease.

8.4 The programme

The system was operated on a standard personal computer with Microsoft Windows 3.1, and Microsoft Access 2.0 or higher. The hardware used to run the program needed at least 8 Mb of RAM and approximately 65Mb of hard disk space. On opening the database, operators may select tables, forms, reports and queries about data already entered into the system.

8.5 Commands and data entry

It is beyond the scope of this chapter to discuss in detail the development of the database itself. However, Access has detailed 'Help' facilities and 'Wizard' functions which provide step by step instruction in a number of activities within the program. Once the operator is familiar with the programme, operation of Access is relatively straightforward. A number of hospitals and educational

establishments offer instructional courses in the operation of Access while many others have computer help desk facilities.

Once the database has been set up, the practical application of the database is relatively simple to operate. Staff can be trained to use the database in a matter of minutes. Following data entry, Access will run queries and produce reports. Data may also be copied to Microsoft Excel for numerical and statistical evaluation if required.

8.6 Involvement in the 'Green Card' scheme

Details of ADR reports were entered into HAROLD from the data collection forms. From this data, HAROLD automatically produced a number of pre-programmed reports:

- A summary of 'Green Card' ADR reports for the Trust's 'Drug and Therapeutics Committee'. This provided a brief description of each ADR reported via the 'Green Card' scheme, the suspect drugs, whether or not they are under intensive CSM / MCA surveillance, and whether a Yellow Card had been sent to the CSM / MCA. The reporter's profession was also included.

- An acknowledgement letter to the reporter. This provided basic background information to their suspected ADR including the number of CSM / MCA reports of the ADR and whether the reaction was well documented or otherwise. Where appropriate, reporters were also advised as to whether a report has been sent to the CSM / MCA via the Yellow Card Scheme. As

stated earlier, it was felt that provision of such information is vital in encouraging staff to continue their participation in the scheme.

- An information sticker was generated by the database. This was placed on the cover of patients' medical records to alert hospital staff that the patient may be sensitive to a particular drug and that a letter giving further details of the reaction may be found inside the medical records. In the event of the letter being lost or removed, the stickers also carry an ADR reference number which may be used to obtain further details from the pharmacy department.

- A letter to be placed inside the patient's notes advising potential prescribers of the nature of the ADR. This letter also included a reference number with which the reader may obtain further details of the ADR from the Pharmacy Department.

- A letter to the patient's GP advising them of the patient's details, details of the ADR and the suspect drug. Similarly, the telephone number of the department's drug information department and an ADR reference number were provided for the GP to make further enquiries if necessary.

- A 'Yellow Card' substitute was generated by the computer for reports that needed to be forwarded to the CSM / MCA. All information fields listed on official Yellow Cards were included in the computer generated report. A contact number and ADR reference number were also included in the report so that further information may be obtained from the Pharmacy department

on request. Since the introduction of HAROLD a number of such reports have been submitted to the CSM / MCA.

- A sticker was also produced which was placed on a card similar to those used in patient medication record registration cards. This is given to the patient to show to their doctor, dentist or pharmacist when receiving medication in the future. This aimed to prevent the patient being re-exposed to medicines to which they have previously suffered an ADR.

Data entry may be performed in a matter of minutes. All reports may be subsequently generated by HAROLD in a fraction of the time required to produce the same reports manually.

8.7 Other uses

HAROLD was also designed to be used to detect trends in ADR reporting and reporter status and to analyse data where appropriate. It was anticipated that the improvements made to the 'Green Card' scheme, the use of HAROLD and the information provided to the hospital staff and GPs, would encourage further involvement in ADR reporting by all concerned.

8.8 Future uses

Future developments for the program may include the interfacing of HAROLD with on-line information, for example, the British National Formulary, Martindale, the Internet, the CSM / MCA database and Medline. This would allow faster and perhaps more efficient literature searching to be performed for ADR related

queries and would save time consuming and often tedious tasks. This may be particularly true if more than one drug is suspected of causing the reaction or alternatively, if a suspect drug is not easily identified from a patient's symptoms.

Chapter 9:

Evaluation of changes to an in-hospital ('Green Card') adverse drug reaction reporting scheme

Chapter 9: Evaluation of changes to an in-hospital ('Green Card') adverse drug reaction reporting scheme.

9.1 Introduction.

Local schemes serve a number of purposes which have been described in Chapter 2. If the reported incidences of ADRs experienced by hospital in-patients and ADR related hospital admissions are compared to the number of patients treated by the hospital each year, then it is likely that there is a large number of ADRs occurring in the hospital that are never reported and subsequently identified by the in-house scheme.

In order to tackle the problem of under reporting, changes to the 'Green Card' scheme were implemented (detailed below). This chapter describes the impact of these changes and the evaluation of the reports received by the scheme.

9.2 Methods.

The 'Green Card' scheme was introduced in 1985 and shortly after, wall mounted holders for 'Green Card' report forms were issued to all wards. However, it became apparent that few of these holders remained in their original position and that little had been done to promote the scheme for a number of years. In December 1996, the following changes were made to the ADR reporting scheme in an attempt to improve the numbers of reports received;

- Re-issuing wall mounted 'Green Card' report form holders with attached, explanatory posters, to all wards and clinics at the hospital (Appendix 5).

- Placing of a reminder to report suspected ADRs, on the front cover of all British National Formularies issued by the pharmacy department.
- Distribution of a Drug and Therapeutics Committee newsletter discussing the purpose of, and promoting the 'Green Card' scheme.
- Recruitment of specialist nurses for a nurse reporting study with reports being forwarded to the 'Green Card' scheme.
- Holding a short training and awareness session for doctors and for pharmacists who were asked to promote the scheme.
- Promotion of the scheme in the hospital formulary.

All reports were entered onto the HAROLD computer database and both an experienced clinical pharmacist and a clinical pharmacologist assessed each report. Use of two algorithms to determine the likelihood a reaction had occurred was considered more scientific than the use of global introspection. For a subjective approach, Venulet and Ten Ham's algorithm (a series of semi structured questions) was used.[57] For an objective approach, Naranjo's algorithm (a series of rigid, closed questions) was used.[54] This involves the calculation of a score for each reaction which is then compared to a banded list of likelihoods that reactions have occurred, for example, probable or unlikely. Data were further categorised with regard to:

- Classification of the organ system affected by the ADR using a classification method obtained from the CSM / MCA Mersey Regional Monitoring Centre (unpublished).
- Drug class using the categories listed in the British National Formulary.[17]
- Severity (serious / non-serious)[17]

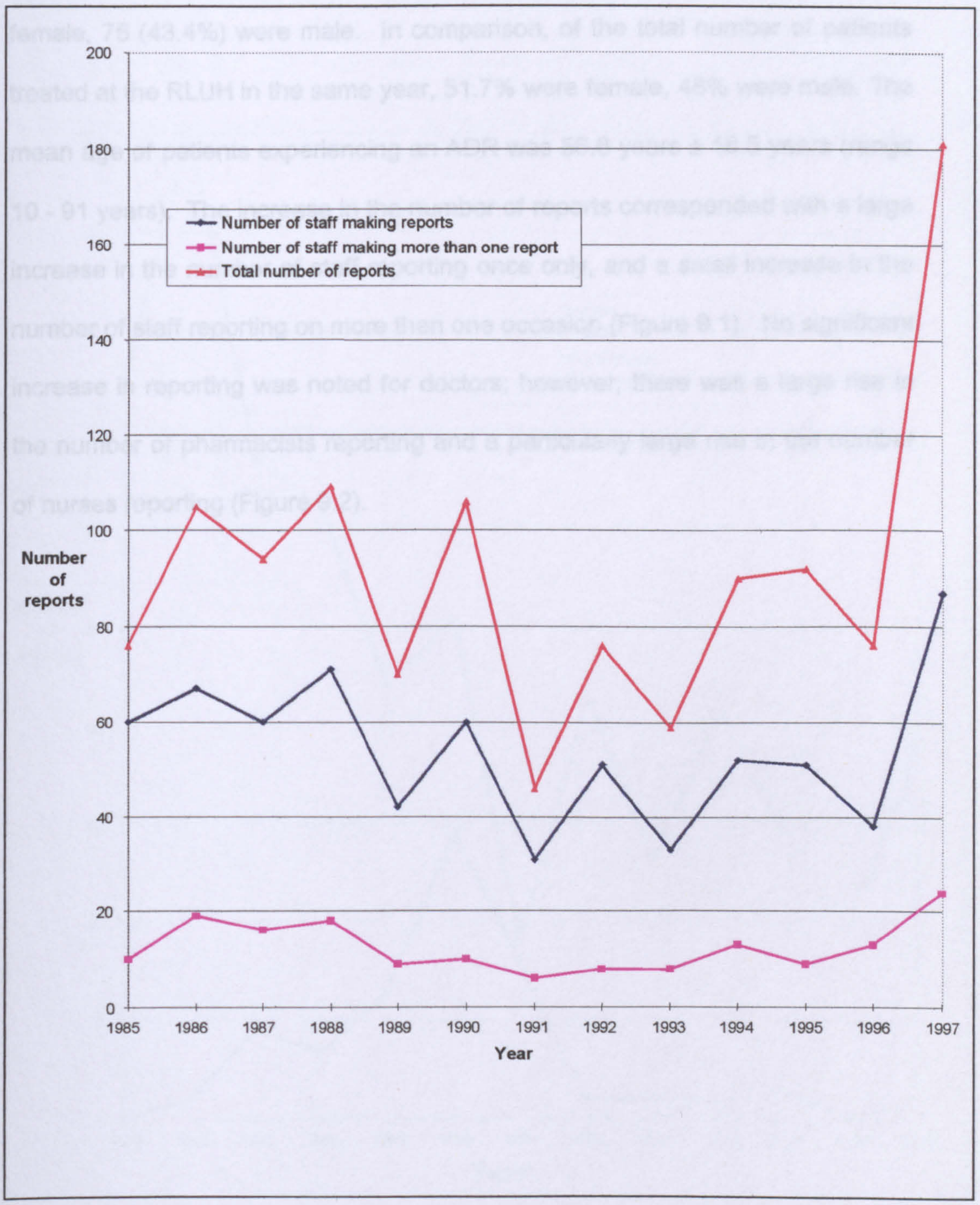
- Causality (the likelihood a reaction had occurred [Ten Ham's[57] and Naranjo's[54] methods])
- Whether the reaction was a type A or a type B reaction[120]
- Origin of the report (profession, speciality and location)
- Whether the product was under intensive post marketing surveillance (black triangle scheme)
- Whether the report resulted in a Yellow Card report to the CSM / MCA

Correlation between the two causality ratings was determined by Spearman's rank correlation. Reactions were assessed and classified independently for each category. Data were exported to Epi Info Version 6.0 for statistical analysis including simple frequency evaluations and cross tabulations employing chi squared tests.[67] P values of 0.05 or less were considered to be statistically significant.

9.3 Results.

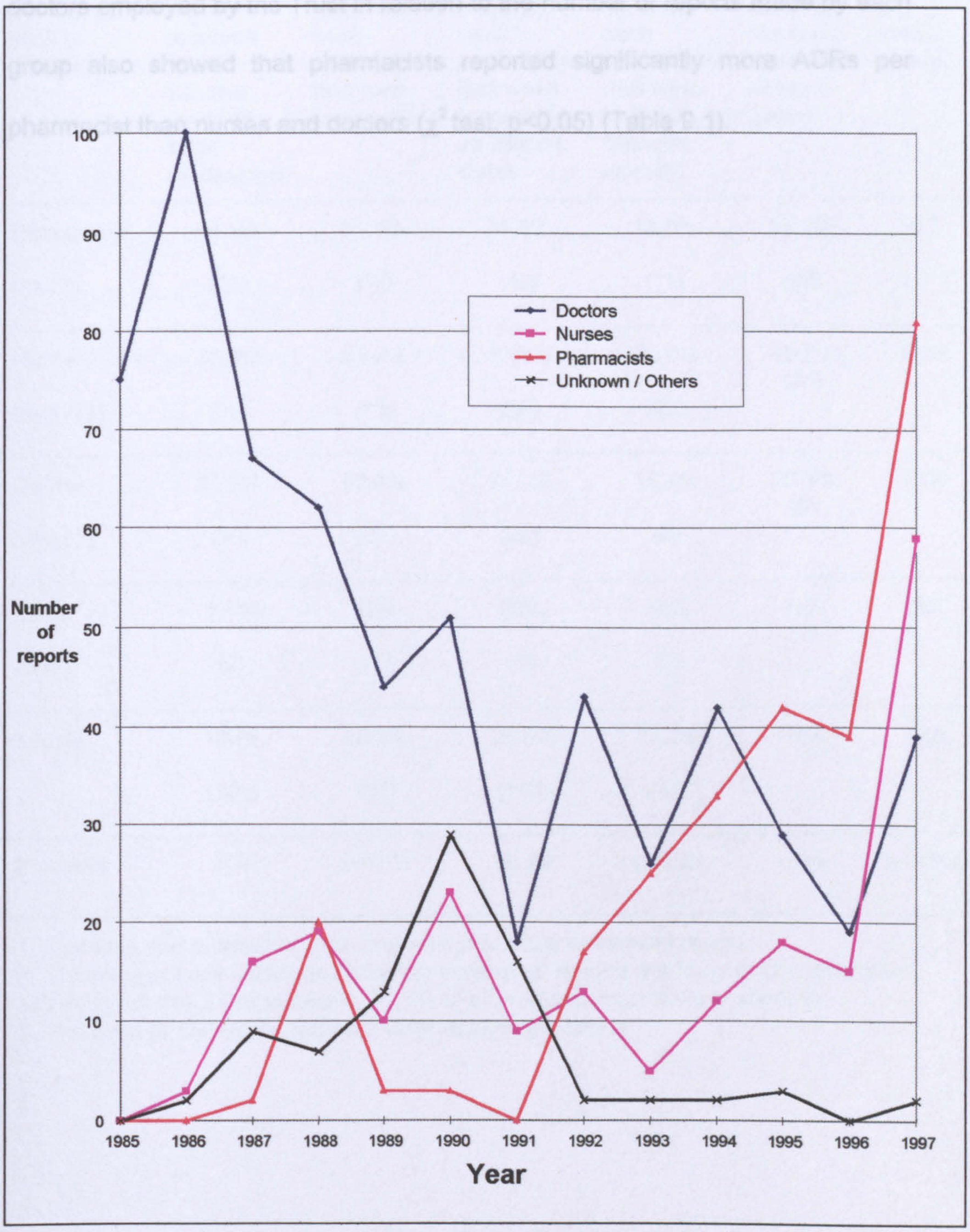
Reports were analysed for 1997 in which a total of 181 reports were received by the scheme compared to an average of 84 reports for each of the previous 11 years (Figure 9.1).

Figure 9.1: Number of ADR reports received by the 'Green Card' scheme at the RLUH since it began in 1985



Of the patients experiencing ADRs that were reported, 102 (57.6%) were female, 75 (43.4%) were male. In comparison, of the total number of patients treated at the RLUH in the same year, 51.7% were female, 48% were male. The mean age of patients experiencing an ADR was 56.6 years ± 18.5 years (range 10 - 91 years). The increase in the number of reports corresponded with a large increase in the number of staff reporting once only, and a small increase in the number of staff reporting on more than one occasion (Figure 9.1). No significant increase in reporting was noted for doctors; however, there was a large rise in the number of pharmacists reporting and a particularly large rise in the number of nurses reporting (Figure 9.2).

Figure 9.2: Number of 'Green Card' ADR reports made by individual professions per year



Cross-checking established that no duplicate 'Green Card' reports were received by the scheme in 1997. Analysis of the number of pharmacists, nurses and doctors employed by the Trust in relation to the number of reports made by each group also showed that pharmacists reported significantly more ADRs per pharmacist than nurses and doctors (χ^2 test, $p<0.05$) (Table 9.1).

Table 9.1: 'Green Card' ADR reports: Breakdown by profession.

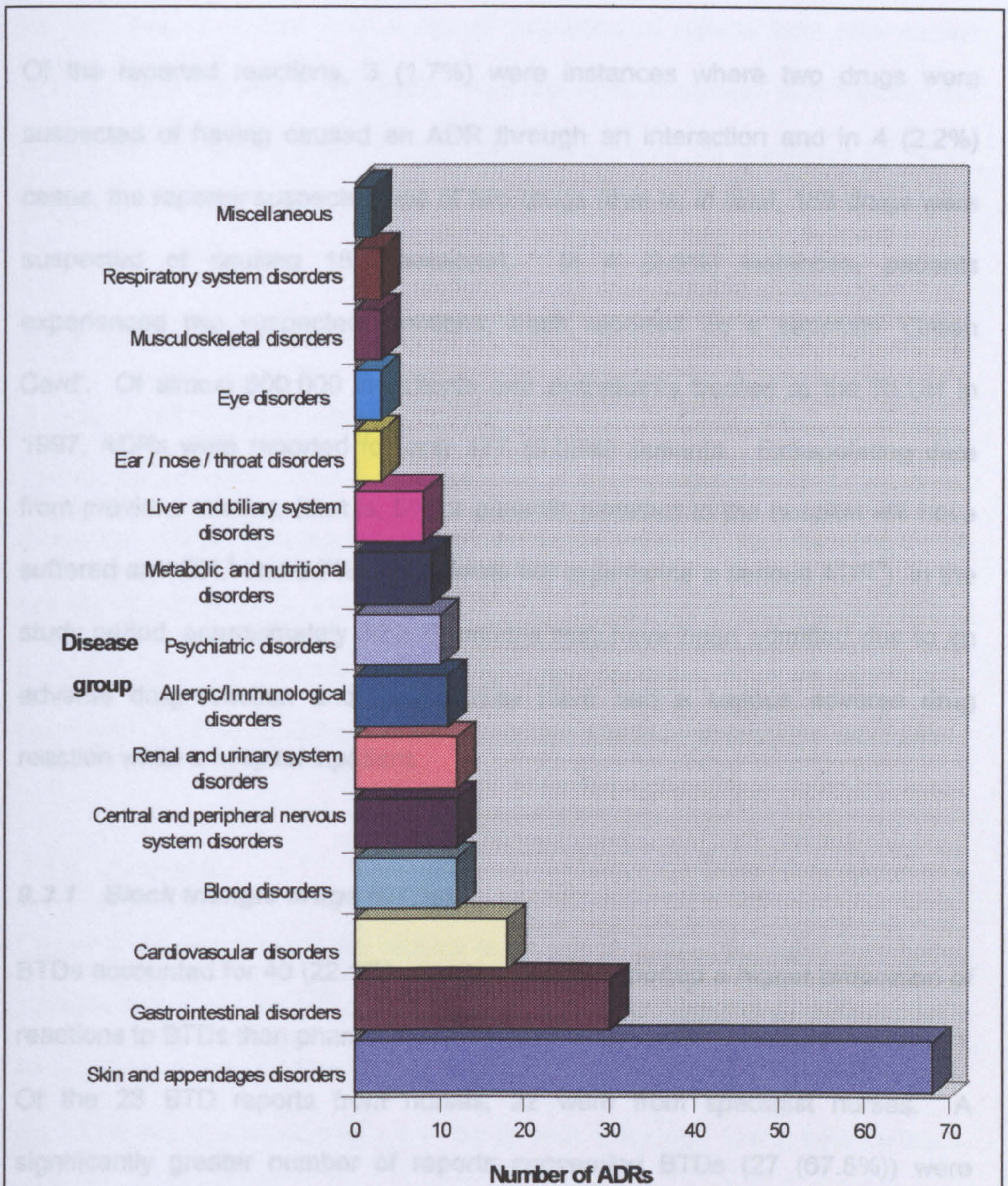
Profession (n= No. of staff in RLUH)	% of the total reports received by the scheme made by each profession	% of reports made by each profession that were 'serious'[2]	% of reports made by each profession that were forwarded as Yellow Cards[2]	% of reports made by each profession that were to black triangle agents[2]	% of reports made by the top 3 reporters in each group	No of reports per staff group.
Pharmacist (n=17)	44.8% (81)	61.7% (50)	51.9% (42)	13.6% (11)	51.9% (42)	4.7
Nurse (n=1723)	32.6% (59)	32.2% (19)	67.8% (40)	39.0% (23)	40.7% (24)	0.03
Doctor (n=417)	21.5% (39)	53.8% (21)	56.4% (22)	15.4% (6)	20.5% (8)	0.09
Other[1] (n=2)	1.1% (2)	50% (1)	50% (1)	50% (1)	N/A	N/A
Totals[3]	100% (181)	50.3% (91)	58.0% (105)	22.7% (41)	N/A	N/A
P values	NA	p<0.01	p0.22	p<0.01	N/A	p<0.0001

1. Includes one aromatherapist and one pharmacy technician report.
2. Percentages are calculated from the number of reports made by each profession shown in column 2 (for example, 61.7% of pharmacist reports were serious)
3. Percentage calculated from the total number of reports.

Reports were made by 89 members of hospital staff, that is, less than 4% of those eligible to do so. Of the reports, 63 (34.8%) were made by the top 5 reporters in the hospital (three pharmacists and two (specialist) nurses). The

substantial influence of the three most frequent reporters for each profession is illustrated in Table 9.1. For pharmacists, over half (51.9%) of the reports received came from three of those reporting, for nurses, 40.7% came from three reporters but for doctors, the proportion was much less (20.5%). Of the 52 wards and clinics from which reports arose, over half (54.7%) came from just 12 units (23%). In terms of specialities within the hospital, the 'Medicine' and 'Surgery' directorates accounted for the majority of the reports (51.4%), reflecting the distribution of the Trust's case mix. 'Skin and appendages' and 'gastrointestinal' reactions accounted for 98 (54.1%) reports while the remainder were divided between 13 other classes of reaction (Figure 9.3).

Figure 9.3: Number of reports per disease group



Of the reported reactions, antibacterial drugs accounted for 33 (17.5%) reactions, antiviral drugs for 14 (7.4%) reactions, anti-depressant drugs for 13

(7.0%) reactions and drugs used in rheumatic diseases and gout, for 11 (5.9%) reactions. The remainder was divided between 27 different categories of drugs.

Of the reported reactions, 3 (1.7%) were instances where two drugs were suspected of having caused an ADR through an interaction and in 4 (2.2%) cases, the reporter suspected one of two drugs (that is, in total, 188 drugs were suspected of causing 181 reactions). In 4 (2.3%) instances, patients experienced two suspected reactions, each reported on a separate 'Green Card'. Of almost 600,000 in-patients and outpatients treated at the RLUH in 1997, ADRs were reported for only 177 (0.03%) patients. Extrapolating data from previous studies, (that is, 5% of patients admitted to the hospital will have suffered an ADR,[4] and 6.7% of inpatients will experience a serious ADR[5]), in the study period, approximately 30,000 patients may have been admitted due to an adverse drug reaction and 40,200 may have had a serious adverse drug reaction while a hospital inpatient.

9.3.1 Black triangle drugs (BTDs).

BTDs accounted for 40 (22.1%) reports. Nurses reported a higher proportion of reactions to BTDs than pharmacists and doctors (χ_2 14.09, $p<0.001$) (Table 9.1). Of the 23 BTD reports from nurses, 22 were from specialist nurses. A significantly greater number of reports concerning BTDs (27 (67.5%)) were classified as 'serious' in comparison to non-black triangle drugs (65 (46.8%)) (χ_2 5.71, $p=0.02$). All 40 BTD reports were reported to the CSM / MCA as Yellow Cards.

9.3.2 'Serious' and 'Non-serious' reactions.

Using CSM / MCA criteria, 91 reactions were judged as being 'serious' and 90 as 'non serious' (Table 9.1). A higher proportion of reports from pharmacists (61.7%) were classified as 'serious' reactions when compared with reports from nurses (32.2%) and doctors (53.8%) although this was not significant (χ^2 14.12, p=0.07).

9.3.3 Yellow Card reports.

A total of 105 Yellow Cards were sent to the CSM / MCA (Table 9.1). A higher percentage of reports from nurses were forwarded to the CSM / MCA as Yellow Cards than those from doctors and pharmacists, although the differences were not significant (χ_2 5.73, p=0.22) (Table 9.1). Of the Yellow Card reports sent to the CSM / MCA as a result of the 'Green Card' scheme, two were identified by the CSM / MCA as duplicates, having been submitted directly by the reporters.

9.3.4 Causality.

Causality assessment of the reports is shown in Tables 9.2 and 9.3. Using Venulet and Ten Ham's[57] and Naranjo's[54] methods, significant differences in causality were observed between the different professional groups that reported (χ_2 20.24 and 13.8 respectively, p=0.03 for both methods). Using both methods, nurses reported the highest proportion of 'probable / likely' or 'definite' reactions (76.2% and 55.2%) in comparison to pharmacists (61.8% and 43.8%) and doctors (43.7% and 23.1%). A significant correlation was observed between the 2 methods of causality assessment (R_s value of 0.6 ($p<0.001$)) indicating a degree of consistency between the two methods.

Table 9.2: Classification of likelihood that an ADR had occurred by reporters profession using Venulet and Ten Ham's method.

Reporters status	Certain	Probable / Likely	Possible	Unlikely	Conditional / Unassessable	Unlikely / Unassessable
Doctors (n=39)	7.7% (3)	36.0% (14)	25.6% (10)	5.1% (2)	17.9% (7)	7.7% (3)
Nurses (n=59)	8.5% (5)	67.7% (40)	15.3% (9)	0.0% (0)	6.8% (4)	1.7% (1)
Pharmacists (n=81)	19.8% (16)	42.0% (34)	16.0% (13)	4.9% (4)	11.1% (9)	6.2% (5)
Others (n=2)	0.0% (0)	50% (1)	0.0% (0)	0.0% (0)	50% (1)	0.0% (0)
*Total (n=181)	13.3% (24)	49.2% (89)	17.6% (32)	3.3% (6)	11.6% (21)	5.0% (9)

Percentages are calculated from the number of reports made by each profession, that is, the n values in column 1 (for example, 7.7% of doctors reports were 'Certain')

*Percentage calculated from the total number of reports.

Table 9.3: Classification of likelihood that an ADR had occurred by reporters profession using Naranjo's method.

Reporters status	Definite	Probable	Possible	Unlikely
Doctors (n=39)	0.0% (0)	23.1% (9)	74.4% (29)	2.6% (1)
Nurses (n=59)	5.1% (3)	50.1% (30)	47.5% (28)	0.0% (0)
Pharmacists (n=81)	3.7 (3)	40.1% (33)	55.6% (45)	0.0% (0)
Others (n=2)	0.0% (0)	50% (1)	50% (1)	0.0% (0)
***Total (n=181)**	3.3% (6)	40.3% (73)	56.9% (101)	0.55% (1)

*Percentage calculated from the total number of reports.
Percentages are calculated from the number of reports made by each profession, that is the n value in column 1 (for example, 23.1% of doctors reports were 'Probable')

9.3.5 Type A and B reactions.

Of the reported reactions, 89 (49.2%) were type A and 92 (50.8%) were type B reactions. There was no significant difference in the proportion of type A and type B reactions that were attributed to black triangle and non black triangle drugs (p=0.2). Similarly, there was no significant difference between the proportion of type A or B reactions that resulted in Yellow Cards (p=0.7). Of the type A reactions 45 were 'serious', 44 'non serious' and of the type B reactions 47 were 'serious' and 45 'non serious'. A larger proportion of reports from

pharmacists were type A reactions when compared with reports from doctors who reported a larger proportion of the type B reactions (Table 9.4).

Table 9.4: Type A and B reactions by profession

Professional status	Type A reactions (%)	Type B reactions (%)
Doctors (n=39)	11 (28.3%)	28 (71.7%)
Pharmacists (n=81)	48 (59.3%)	33 (40.7%)
Nurses (n=59)	30 (50.8%%)	29 (49.2%)
Others (n=2)		2 (100%)

Overall, a significant difference was observed between professions (χ_2 = 10.2, p=0.006) suggesting that pharmacists were more likely than doctors or nurses to report ADRs of a pharmacological nature.

9.4 Discussion.

The 'Green Card' scheme has been criticised in the literature as being 'cumbersome' and 'not the way forward'.[101] However, experience suggests that the scheme increases reporting via national pharmacovigilance schemes and encourages awareness of the importance of reporting ADRs amongst the hospital staff. While gross underreporting of ADRs is a problem that the 'Green Card' scheme has only partly addressed, development of the scheme has

increased reporting across the professions and allowed some analysis of reporting trends within the Trust. The development of an 'ADR reporting culture' has been suggested as a method of encouraging reporting and increasing awareness of ADRs.[20] This issue has been addressed in the USA where hospitals are required by the Joint Commission on Accreditation of Healthcare Organisations to have procedures for reporting ADRs.[46]

The results of this study show that by promoting in-house or local ADR schemes, it is possible to increase the number of reports received by such schemes, to encourage individual staff members to report via the scheme and to encourage staff to report more than once. This was achieved largely by the use of passive methods of promotion, which did not have a significant impact on the workload of the staff operating the scheme. However, given the incidence and importance of ADRs, departments should consider committing resources to this area. The results demonstrate that motivated individuals can make a significant contribution to ADR reporting. Enlisting staff on each ward or clinic to act as a facilitator for reporting and targeting them with bulletins and information to encourage ADR reporting by their colleagues may be a development which could significantly enhance ADR reporting rates.

Pharmacists reported a high number of ADRs in comparison to doctors or nurses. Given that the proportion of 'unlikely' or 'possible' reports for pharmacists (20.9%) was lower than that for doctors (30.7%) and marginally higher than that for nurses (15.3%), it does not appear that pharmacists were 'trigger happy' in their approach. The majority of reports from pharmacists were of type A reactions while in contrast, doctors appeared to report more type B

reactions. This suggests that pharmacists might be prepared to report more well known or predictable reactions than doctors who tend to report more unusual or unexpected reactions. Nationally, a comparison of hospital pharmacist and hospital doctor Yellow Card reports has identified a similar pattern.[83] This difference in reporting is unlikely to have been influenced by the severity of the reaction, given that type A and B reactions identified in this study were of equal severity and that doctors and pharmacists reported similar proportions of serious reactions.

The contribution that nurses made to the 'Green Card' scheme was substantial, and is in accordance with another study.[70] The higher number reports to BTDs made by nurses was largely due to two specialist nurses. The potential contribution of specialist nurses is evident and should be explored further. From the results, it is clear that other than doctors, nurses and pharmacists, few professions are inclined to participate in the scheme. Within those professions willing to participate, a minority of staff in each group appears to make the majority of the reports received by the scheme. Few reports were received from radiologists and anaesthetists and few reports were received from operating theatres and the accident and emergency department. Potential for expansion of the scheme to other professions, sub sections of medical and nursing staff and to clinical areas clearly exists.

Causality assessment by the methods of Venulet and Ten Ham, which is based on a 'best fit' categorisation, was preferable to Naranjo's algorithm with the reports studied, because of the flexibility that it afforded in judging some reactions. Reactions that were evidently 'unlikely' or 'unassessable' using

Venulet and Ten Ham's method could still be classified as 'possible' by Naranjo's method, and thus the former method was found to be more applicable to reports received by the scheme. It is not the aim of the scheme to promote reporting of only 'certain' or 'probable' ADRs, as hospital staff are asked to report all of ADRs. However, it is encouraging to note that of the 151 reactions fully assessed for causality (using Venulet and Ten Ham's method), around three quarters were classified as being 'probable' or 'certain'.

Antibacterial drugs were the most frequent class of drug reported in the scheme and this is not surprising given the frequency of their use in general, acute hospitals. However, of the 33 reported reactions to antibacterial drugs, 23 (69.7%) were non-serious (18 reports of skin rashes, (54.5%) and 4 reports of gastrointestinal tract disturbances (12.1%)). In comparison, 9 (81.8%) of the 11 reactions reported for Drugs used in Rheumatic Diseases and Gout were classified as 'serious'. Few reports were received for cytotoxic agents, this is probably due to the fact that these drugs are regarded as being inherently toxic and staff do not consider serious, albeit well recognised reactions unusual enough to report. For many other drugs for which ADRs might be expected, for example, sulphasalazine, amiodarone or methotrexate, no reports were received, while staff seem to be willing to invest time in reporting rashes and gastrointestinal upsets secondary to antibiotics. Targeting individual drug groups may be of use; however, previous work investigating the highlighting of black triangle drugs failed to show any significant increase in reporting.[48,49] It is possible that practical systems will be unattainable until computer-based prescribing systems are an integral component of the prescribing of drugs in hospital and ADR reporting pathways as part of their capability.

Issues concerning quality within the NHS are currently increasing in profile as the concepts of clinical governance and risk management gain momentum. Other work has shown many ADRs to be predictable and either preventable or manageable.[82,102] It has also been demonstrated that inappropriate use of medicines is a major cause of ADRs.[81] Use of data from local schemes could be used to evaluate the impact that ADRs have on the quality of clinical care within the NHS, and perhaps provide avenues to decrease their incidence. Such data would enable hospitals to target resources to the areas in which they might be expected to have most impact. Risk management also extends to preventing inadvertent re-exposure of a patient to a drug suspected of having been responsible for the ADR in the past.[10,79,73] The concept of clinical governance has been introduced with the intention of setting standards concerning the management of clinical situations in which the management and reporting of ADRs would appear to be a core issue.[77] Schemes such as the 'Green Card' scheme and the data that they provide will prove to be valuable tools in the endeavour to attain 'clinical excellence'.

9.5 Limitations

Caution should be exercised before extrapolating the findings of the chapter to other institutions. The presence of the principal researcher and the knowledge that the study was contributing to a research project could have encouraged pharmacists at the RLUH to increase their contribution to the scheme beyond that which might have been identified under other circumstances. The principal researcher also contributed to the ADR reports received by the scheme and although the number of reports concerned was not among the highest in terms

of reports per individual, this introduces potential bias into the research. The influence of individuals motivated to contribute to the scheme is illustrated in Table 9.1 and should be considered when considering the application of the findings of this research elsewhere. The existence of the scheme prior to its 'relaunch' is another factor that should be considered since it is likely that many of those who reported ADRs via the 'Green Card' scheme were aware of its existence before this assessment was carried out.

Chapter 10:

Communication regarding ADRs between secondary and primary care: A postal questionnaire survey of general practitioners.

Chapter 10: Communication regarding ADRs between secondary and primary care: A postal questionnaire survey of general practitioners.

10.1 Introduction.

The 'Green Card' scheme has been described in the previous chapter and in Chapter 2. Previous audit work at the trust demonstrated that a number of ADRs were neither documented in patients' notes nor communicated to patients' general practitioners, even for serious reactions.[73] As part of efforts to increase the profile and effectiveness of the in-house 'Green Card' scheme, it is proposed that GPs should be issued with a notification form and patients issued with an ADR warning card and / or an ADR notification form.

10.2 Aims

The aim of this study was to survey general practitioners within the health authority in which the Trust is situated to ascertain their views on the current transfer of data concerning ADRs and to gauge their opinions on the proposed scheme to improve communications between the GP, patient and the hospital.

10.3 Methods.

A structured questionnaire using a combination of open and closed questions was designed. Issues relating to communication of data concerning ADRs from secondary to primary care and the provision of information to patients were included. The questionnaire, a covering letter, a sample notification form

(Appendix 6) and a prepaid return envelope were sent to all general practitioners within Liverpool Health Authority. One month later, follow up letters and questionnaires were redistributed. Data were collated and analysed using Microsoft Access version 7.0.

10.4 Results.

Of the 270 general practitioners surveyed, 141 (52.2%) responded. Not all questions were answered by each respondent. When asked how often they saw patients who had experienced an ADR while in hospital, a high proportion (46 (33.1%) reported seeing such patients 'occasionally' and 4 (2.9%) reported it as a 'frequent' occurrence (Table 10.1). Of the 114 (88.4%) respondents who saw such patients, 60 (52.6%) felt that instances where no record of the ADR existed in patients' discharge documentation happened 'occasionally' while a further 15 (11.6%) stated that this occurred frequently. (Table 10.1).

Table 10.1: Summary of general practitioners responses

	Frequently	Occasionally	Rarely	Never
How often GPs see patients who have suffered an ADR while a hospital in-patient. (n=139)	2.9% (4)	33.1% (46)	54.6% (76)	9.4% (13)
How often the patient tells the doctor they have suffered an ADR but no record exists in their discharge documentation. (n=129)	11.6% (15)	46.5% (60)	30.2% (39)	11.6% (15)
How often can patients name the exact drug to which they have previously suffered and ADR. (n=118)	6.7% (8)	24.6% (29)	58.5% (69)	10.2% (12)
How often can the patient describe the exact nature of the reaction they suffered? (n=118)	30.5% (36)	39.8% (47)	28.8% (34)	0.9% (1)
How often is insufficient information supplied in the discharge documentation? (n=133)	22.6% (30)	37.6% (50)	31.6% (42)	8.2% (11)
How often is the total information from the patient and discharge documentation insufficient to make an informed decision about the consequences of an ADR? (n=134)	23.3% (31)	45.5% (61)	25.3% (34)	6.0% (8)

10.4.1 Confidence in information provided by patients.

GPs were asked how often they thought patients could name the exact drug to which they had suffered an ADR. A high percentage (81 (68.7%)) stated that patients could 'rarely' or 'never' name the drug (Table 10.1). Fewer GPs (35 (29.7%)) felt that patients were unable to describe the nature of their reaction (Table 10.1). GPs were asked how confident they were in the information that patients gave them. None were 'very confident' in this information while 92 (78.6%) were 'uncertain' or 'very uncertain' of this information. A lack of written information and uncertainty in verbal information from patients may make it difficult for GPs to determine the significance of an ADR a patient has experienced in hospital. Almost half of the respondents (61 (45.4%)) stated that instances where they had insufficient information to make an informed decision about an ADR was an 'occasional' occurrence. A further 31 (23.1%) thought that this situated was a 'frequent' event (Table 10.1).

10.4.2 Additional information required in the ADR notification form.

The majority of GPs were satisfied with the content of the ADR notification form. Only 2 (1.4%) GPs stated that some information provided was unnecessary; 108 (76.5%) stated that no further additional information was required. In response to an open question, 42 (29.8%) GPs thought that additional information was required, the nature of which is listed in Table 10.2.

Table 10.2: Additional information requested by GPs for notification form.

Additional information	Frequency of request.
Dates and duration of reaction	5
Further advice (management / further action)	5
Information given to patient	5
Clinical indication for drug	4
Other drugs	4
Treatment for ADR	4
Severity	4
Causality	3
Rechallenge	3
Dose	2
Type A or Type B reaction	2
Outcome	1

Typical comments included:

"Dosage, need for further follow up or action. Related drugs which should be used with caution."

"Exact nature of adverse reaction, nature of drug concerned, antidote if given"

"How confident is the diagnosis - should the drug be avoided or used with caution."

"Is the ADR consistent with manufacturers published side effect profile? Type of reaction e.g. allergic, idiosyncratic, toxic or drug interaction."

"Relevance to future management"

"Severity of reaction, any treatment given at the time, information given to patient, any follow up necessary by GP."

"Whether the patient should ever take the same or same class of drug ever again."

10.4.3 Should patients receive a copy of the ADR notification form?

Regarding the notification form, 110 (82.7%) respondents thought that patients should get a copy (n=133). However, when asked to comment, GPs had mixed views about this proposal (Table 10.3).

Table 10.3: Should patients receive a copy of patient notification form

Should patient receive card: Comment	Number of respondents
Yes: Seen by different doctors	30
Yes: Patient education	30
Yes: Patient responsibility	7
Yes: Time delay	5
Yes: Improving communication	5
Yes: Prevents litigation	4
Yes: Right to know	3
Yes: Arrange Medic Alert bracelet	2
No: Cause anxiety or alarm	6
No: Increases litigation	4
No: Card better	3
No: Not able to understand	2
No: No need if GP has one	2
No: Patient information leaflet for ADRs	1

Comments in favour included:

"Because sometimes information from the hospital comes late or never at all."

"For their safety in future, in case their medical card goes astray."

"If reaction is severe in case they wish to arrange a Medicaid bracelet or similar"

"It is important that the patient takes responsibility for their health."

"More likely to accept as a significant issue."

"Patent awareness very important. They will often confuse information they are told and it can be difficult then to re-inform with the correct information."

"Patients right to information - they may need this information if they go to a hospital elsewhere."

"So that they can show to other professionals, for example, dentists."

Comments not in favour included:

"ADR card as below probably of more benefit."

"Cause confusion / worry if they do not understand technical terms. They could have a simplified explanation on their discharge letter instead."

"I don't think it is meaningful to the average patient."

"Increases likelihood of litigation."

"Perhaps a more friendly patient information sheet with understandable terminology - less medical."

"They need to have some written information, not necessarily a copy of the form."

"Would like patients to be informed that an adverse reaction had occurred and be able to discuss it if concerned but do not feel giving patients clinical details is helpful."

10.4.4 Providing patients with ADR warning cards.

In response to a proposal to provide patients with a 'credit card' containing the name of the drug to which they have experienced an ADR, 135 (97.8%) of 138 GPs responding thought this would be a useful development with some stating that this would be more appropriate than the notification letter. Comments included:

> *"But they will probably lose it or forget to carry it with them."*
>
> *"Could GPs add to it? - for two way information."*
>
> *"Depends on severity of reaction - a patient could end up with loads of cards for minor ADRs."*
>
> *"How will the card be added to? Will only life threatening ADRs be put on there?"*
>
> *"If there is a severe or unusual reaction perhaps. Otherwise, it seems unnecessary."*
>
> *"Useful for patient to know what to avoid."*
>
> *"Useful in emergencies"*

10.4.5 Inclusion of details of the reaction in the warning card.

It was felt by 99 (76.2%) of 130 GPs responding, that the card should contain details of the reaction the patient experienced. Specifically, 8 GPs stated that the card should contain details of the severity of the reaction, 3 stated there would be insufficient space, 2 suggested including the likelihood a reaction had occurred and 4 stated that the card should briefly describe the reaction. Comments included:

"No need for letter to go to patient in this case."

"Perhaps should include mild / moderate / severe."

"Probably not enough room on the card to be helpful."

"Too much information will confuse or be ignored."

10.4.6 Improving communication.

When asked how else communication of ADR data could be improved, the majority of GPs' comments related to the length of time it takes for discharge correspondence to reach them once a patient has been discharged. Thus, many GPs suggested using the telephone, e-mail or facsimile machines to relay information as soon as the patient is discharged. A further 11 GPs suggested that information should be included in the discharge prescription sheet and 9 suggested this information be included in the discharge letter. Comments included:

"By fax, phone, e-mail if very significant."

"Currently - no great communication, therefore any would be an improvement."

"Do so specially rather than in the typed summary received four or five months later."

"For serious life threatening events, a telephone call to the GP would be helpful."

"It would be helpful if pharmacy could write a discharge summary perhaps listing the drugs which we should be wary of using in a patient who's had an ADR."

"Keep the paper work down."

"Tell patient, make them aware that they also have the responsibility to avoid this drug! Not solely the doctor / pharmacy / hospital role."

"This should be enough - very useful to see if Yellow Card was sent or not."

10.5 Discussion.

GPs perceive consultations with patients who have experienced ADRs while in hospital as a relatively infrequent occurrence. However, on occasions when this occurs, information pertaining to the suspected reaction is often absent from the discharge documentation. GPs perceive that while patients can usually recall the nature of the reaction they experienced, for example, a skin rash or anaphylaxis, they are less likely to recall the exact name of the drug which is thought to have caused the ADR. Furthermore, when GPs are provided with verbal information by their patients, over three quarters of GPs are either uncertain or very uncertain that the information is correct.

Although this study was limited to general practitioners within Liverpool Health Authority for the purposes of the 'Green Card' scheme described earlier, evidence in the literature suggests that that this not a localised problem.[73,79,80] However, care must be taken in interpreting these result in extrapolating them to areas where improved methods of communication may already exist. Previous work has shown that in many instances documentation and communication of data relating to suspected ADRs is neither recorded in patients medical records nor communicated to general practitioners. [73,79,80] The concept of poor

communication between secondary and primary care in terms of both speed and quality is not new and has been described many times in the literature.[103, 104] However, data concerning ADRs is rarely included in these studies. Studies have also demonstrated that, for a number of reasons including poor communication, patients have difficulties managing their medicines post discharge.[105] Understanding and recall of information pertaining to their medicines is, in some cases, worryingly inadequate. Patients that are unable to manage their medicines effectively are at increased risk of therapeutic failure, of ADRs and potentially, readmisson to hospital.

As GPs are unsure of the information that is provided by patients, it is important that written information is sent to general practitioners about ADRs that patients have experienced while in hospital. This issue is also important in terms of risk management in that patients are at risk of being inadvertently exposed to a drug(s) to which they have previously suffered an ADR if GPs and / or the patient themselves are unaware of the name of the suspect drug. Previous work suggests that patients may suffer minor reactions, for example nausea and vomiting and conclude that they are allergic to the drug, when in fact, they are intolerant and could still be prescribed the drug if no other alternatives were available.[106] Methods of communicating such data to patients are not common components of ADR reporting programs.[45] This is a situation which has been addressed using the HAROLD database (see Chapter 8) to generate reports and warning cards. Patients should therefore be provided with written and verbal information and be given the opportunity to ask questions and to address concerns that they may have about an ADR they have experienced. It was of

interest that an equal number of GPs felt that this would either increase or decrease the risk of litigation with regard to ADRs patients may experience.

Many GPs felt that patients should have some written information to show healthcare professionals who may not have access to their medical records, for example, locum doctors or dentists. Provision of written information for use after discharge using a pre-designed form has been discussed in the literature, but again, ADRs were not specifically included in the form.[107] Provision of warning cards need not be a drain on resources and may be as high or low tech as providers wish. The design of the warning card may range from a pre-printed card or dispensing label sealed in a plastic pouch to computer generated plastic cards.

Approval for this development had been received from the Trust's Drug And Therapeutics Committee and also from the Trust's legal department. It is hoped that the scheme will be introduced in the near future. Should the card become integrated into Trust practice, it is hoped that prescribers who want their patients to receive a warning card will be encouraged to report serious ADRs via the in-house 'Green Card' scheme and consequently increase the number of reports.

Chapter 11:

Adverse drug reactions as a cause of admission to an acute medical assessment unit.

Chapter 11: Adverse drug reactions as a cause of admission to an acute medical assessment unit.

11.1 Introduction

Previous work has demonstrated that a significant proportion of hospital admissions are due to adverse drug reactions (ADRs). A review of studies examining ADR-related admissions to hospitals found that on average, 5.5% of all hospital admissions result from ADRs.[4] This incidence varied from 0.2% to 21.7% depending on the population being investigated, for example, elderly populations had a higher rate than for surgical patients. Results of previous, individual studies examining the incidence of ADR related admissions in general medical patients are summarised in Table 11.1.[108,109,110,111,112,113,114,115,116,117,118,119]

Table 11.1: Studies investigating the admission rate due to ADRs.

Study	Year	Study sample	Total admissions	Number of ADR admissions	Percentage ADR admissions
Stanton, Peterson Rumble et al.	1994	Teaching, general medical	691	21	3.0%
Hallas, Gram, Grodum et al.	1992	Teaching, general medical	1999	157	7.9%
Lakshmanan, Hershey and Breslau.	1986	Teaching, general medical	834	45	5.4%
Black and Somers.	1984	Teaching, general medical	481	30	6.2%
Bergman and Wiholm	1981	General medicine	285	16	5.6%
George and Kingscombe.	1980	General medicine	250	10	4.0%
Ghose.	1980	General medicine	171	11	6.4%
Levy, Lipshitz and Eliakim.	1979	Teaching, general medical	2,499	103	4.1%
Wood, Turner and Vere.	1977	General medicine	220	19	8.6%
Wood, Turner and Vere.	1975	General medicine	192	13	6.8%
Hoddinott, Gowdey, Coulter and Parker.	1967	Teaching, general medical	104	3	2.9%
Sidel, Koch-Weser, Barnett and Eaton.	1967	General medicine	267	12	4.5%
Seidl, Thornton, Smith and Cluff.	1966	Teaching, general medical	714	28	3.9%

11.2 Aims

The purpose of this study was to investigate medical patients admitted to a teaching hospital to identify the proportion of admissions that occurred as result of an ADR, and to identify the drugs thought to be responsible for these admissions.

11.3 Method

The study was carried out in the Acute Medical Assessment Unit at a large teaching hospital. The unit was created in 1996 to monitor newly admitted medical patients with the intention of admitting them to an appropriate ward when necessary, or, discharging them for treatment as an out patient or in primary care. Two hundred patients were selected on a daily basis using randomly generated numbers over a period of two months. Information was collected prospectively from newly admitted patients. Data were recorded using a data collection form based on the CSM / MCA Yellow Card adverse drug reaction reporting form and was identical to that used in the 'Green Card' scheme (Appendix 5). Data collected included demographic data, details of concurrent illness, drug history details (including over the counter (OTC) purchases), and reasons for admission to hospital. Any known drug allergies were also recorded. Data were recorded in Microsoft Access Version 7.0 and exported to Epi Info Version 6.0 for analysis. A 'p value' of 0.05 or less was considered to be statistically significant.

Where possible, patients' medication history was verified using the medicines patients had brought into hospital with them. Where an ADR was suspected or

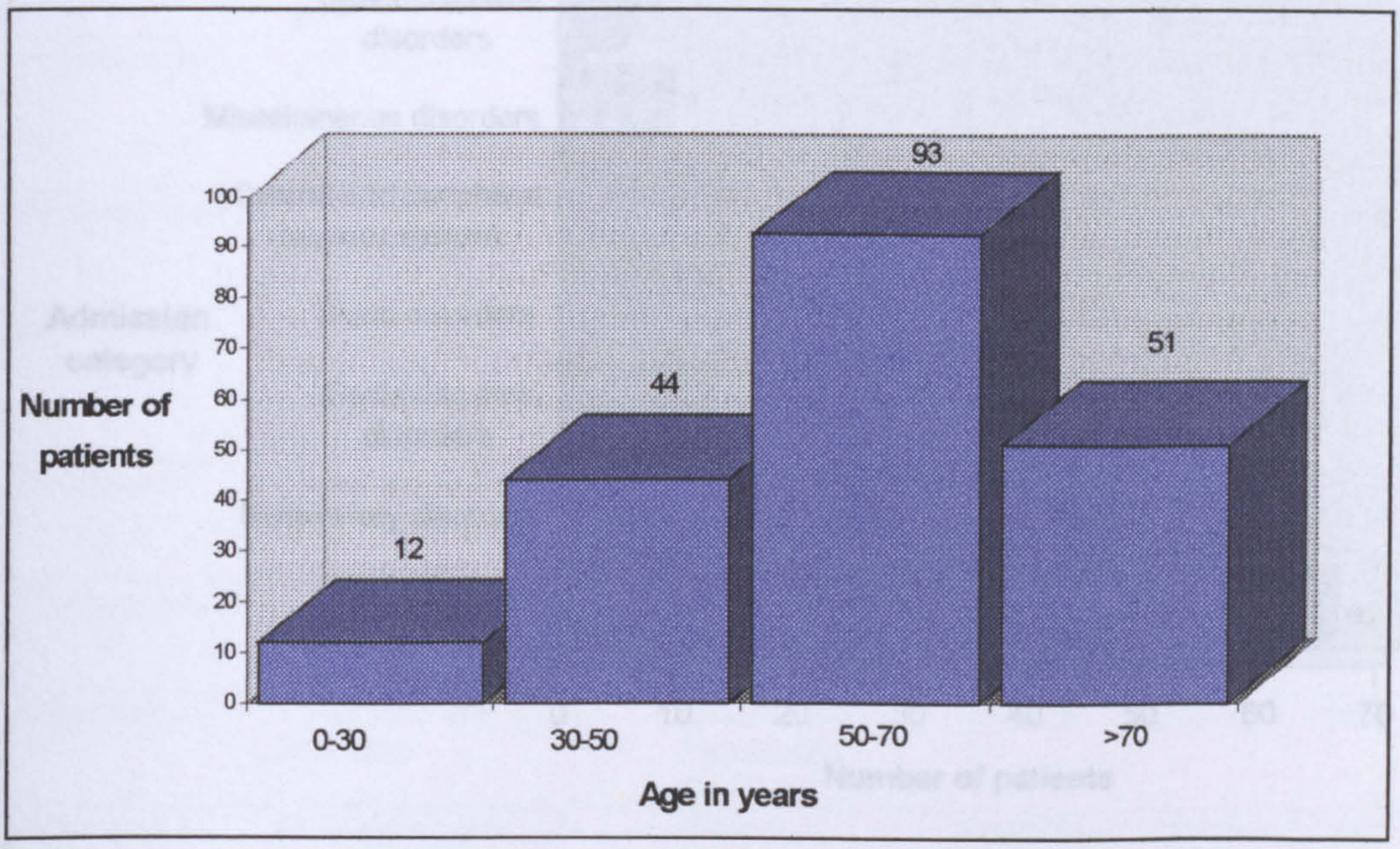
where drug history details appeared to be incomplete, inaccurate or erroneous, the patients' general practitioner was contacted to verify the details of the patient's drug history. For the purposes of this study, an ADR was defined using the World Health Organisation definition: a response to a drug which is noxious and unintended and which occurs at doses normally used in man for the prophylaxis, diagnosis or therapy of disease or for the modification of a physiological function.[1] Adverse effects of drugs due to deliberate self poisoning are excluded from this definition and were not recorded for the purposes of this study.

Patients suspected of experiencing an ADR were followed up five months later to determine the outcome of their admission. ADRs thought to have resulted in hospital admission were reported to the CSM / MCA using a Yellow Card. The likelihood or 'causality' that a reaction had occurred was assessed by an experienced clinical pharmacist and clinical pharmacologist using Venulet and Ten Ham's algorithm [57] and Naranjo's algorithm[54] described in Chapter 9. Reactions were also classified in terms of reaction type (type A or type B) again using previously published criteria.[120]

11.4 Results

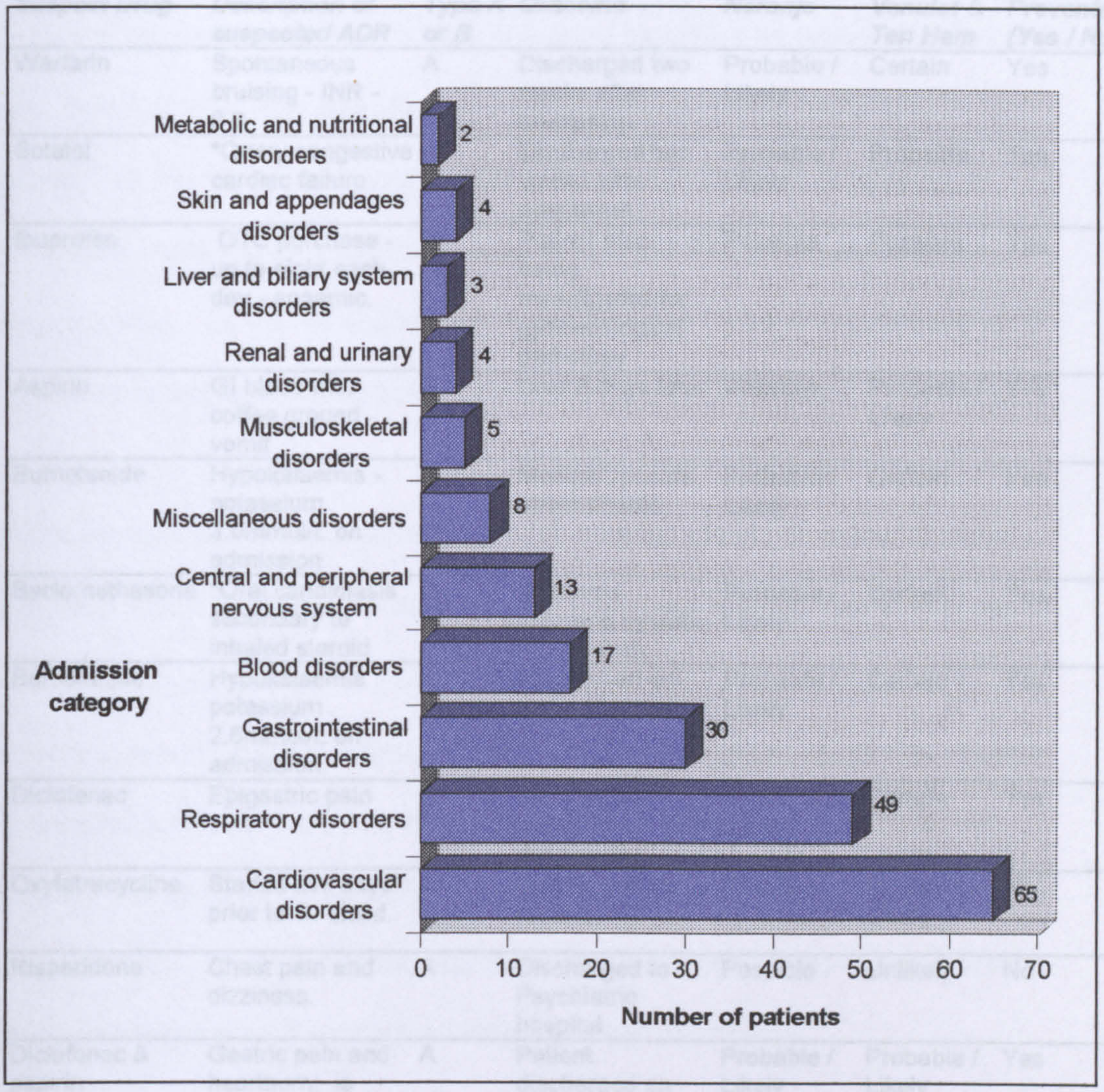
Data were collected for 200 patients of which 107 (53.5%) were males and 93 (46.5%) were females. Ages ranged from 18 to 89 years (mean 58.3 ± 15.8 years, median 62 years), the distribution of which is shown in Figure 11.1.

Figure 11.1: Distribution of age of patients admitted to the Acute Medical Assessment Unit



Of the patients reviewed, 34 (17%) patients described 'drug allergies' including 19 who claimed they were allergic to penicillin, 5 to co-trimoxazole, while the remainder claimed allergies to 13 other medicines. The numbers of drugs patients were taking ranged from 0-13, (mean 3.6 ± 2.78 medicines). The most common reasons for admission to the unit are listed in Figure 11.2.

Figure 11.2: Frequency of reasons for admission to the AMAU



Of the 18 suspected ADRs identified in the study, 15 (83.3%) were judged to be responsible for the patient's admission to hospital and 3 (16.7%) were coincidental to the patients admission. Two patients (1%) died as a consequence of their ADR. The ADRs detected are shown in Table 11.2 together with their causality assessments.

Table 11.2: ADRs detected during study.

Suspect Drug	*Description of suspected ADR*	*Type A or B*	*Outcome*	*Naranjo*	*Venulet & Ten Ham*	*Preventable (Yes / No)*
Warfarin	Spontaneous bruising - INR - 9.2	A	Discharged two weeks after admission	Probable / Likely	Certain	Yes
Sotalol	*Query congestive cardiac failure	A	Discharged two weeks after admission	Probable / Likely	Probable	Yes
Ibuprofen	OTC purchase - up to eight each day - anaemic.	A	Patient also being investigated for gynaecological pathology	Possible	Possible	Yes
Aspirin	GI bleed with coffee ground vomit	A	Died 8 days later	Possible	Probable / Likely	Yes
Bumetanide	Hypokalaemia - potassium 3.0mmol/L on admission	A	Medical records unobtainable	Probable / Likely	Certain	Yes
Beclomethasone	*Oral candidiasis secondary to inhaled steroid	A	Resolved following nystatin mouthwash	Probable / Likely	Certain	Yes
Bumetanide	Hypokalaemia potassium 2.6mmol/L on admission.	A	Discharged on amiloride	Probable / Likely	Certain	Yes
Diclofenac	Epigastric pain	A	Discharged - without diclofenac.	Probable / Likely	Certain	Yes
Oxytetracycline	Started five days prior to GI bleed.	A	Discharged on ranitidine	Possible	Probable / Likely	No
Risperidone	Chest pain and dizziness.	A	Discharged to Psychiatric hospital	Possible	Unlikely	No
Diclofenac & aspirin	Gastric pain and heartburn: is taking	A	Patient discharged on same medication	Probable / Likely	Probable / Likely	Yes
Lisinopril	*Cough - patient on frequent codeine linctus	A	ACE inhibitor withdrawn	Possible	Probable / Likely	No
Frusemide and digoxin	AF secondary to hypokalaemia and digoxin toxicity	A	Died 16 days later	Probable / Likely	Certain	Yes
Propranolol	Congestive cardiac failure and breathlessness	A	Drug withdrawn & treated for CCF	Possible	Possible	Yes
Paroxetine.	Gastrointestinal bleed	B	Patient diagnosed as gastric cancer	Unlikely	Unlikely	No
Ketoprofen.	Exacerbation of congestive cardiac failure	A	Drug withdrawn - patient discharged	Possible	Probable / Likely	Yes
Aspirin	Gastrointestinal bleed	A	Drug withdrawn - discharged on ranitidine	Possible	Possible	Yes
Naproxen.	Gastrointestinal bleed	A	Discharged on ranitidine	Possible	Probable / Likely	Yes

*ADR did not directly result in admission

Using Venulet and Ten Ham's method,[57] of the 15 ADRs thought to have resulted in hospital admission, 10 (66.7%) were identified as being 'probable / likely', and 3 (20%) were classified as being possible. Using Naranjo's method,[54] of the 15 ADRs thought to have resulted in hospital admission, 6 (40%) were identified as 'probable / likely' and 8 (53.3%) were classified as being possible. Of the 18 suspected ADRs, 17 were 'Type A' reactions and 12 (66.7%) were judged to have been predictable and to some extent, preventable.

Patients suspected of experiencing an ADR-related admission were taking a mean of 3.9 (± 1.5) different medicines in comparison to those not suspected of an ADR taking a mean of 3.6 (± 2.9) different medicines (a non significant difference, Mann Whitney U-test, p=0.4). The most common drugs implicated in the hospital admission of patients in this study are shown in Table 11.3. All reactions identified as a possible cause for hospital admission were reported to the CSM / MCA. Only one of the reactions was thought to have been related to a product bought over the counter in a community pharmacy.

Table 11.3: Drugs causing admission - frequency of use.

Drug class	Frequency
Non steroidal anti inflammatory drugs (includes 'low dose' aspirin)	8
Loop diuretics	3
Beta blockers	2
Warfarin	1
Cardiac glycosides	1
Anti-depressants	1
Paracetamol	1

11.5 Discussion

The number of patients identified in this study with ADR related admissions is similar to that found in comparable populations, that is, teaching hospitals / medical admissions. Of particular concern was that 2 (that is 1% of the admissions studied) of the identified ADRs resulted in fatalities. Little work has been done in this area in the United Kingdom, indeed, relatively none in the last ten years, and there is clearly a need for larger studies to be performed. Such research is required to identify practical methods by which the incidence of preventable or predictable adverse drug reactions can be reduced.

None of the ADRs that were identified in this study were reported via the Trust's in-house 'Green Card' reporting scheme and none were recorded in patient's records as being reported to the regulatory authorities (on reporting the ADRs to the CSM / MCA, none were identified as duplicates suggesting that this was the

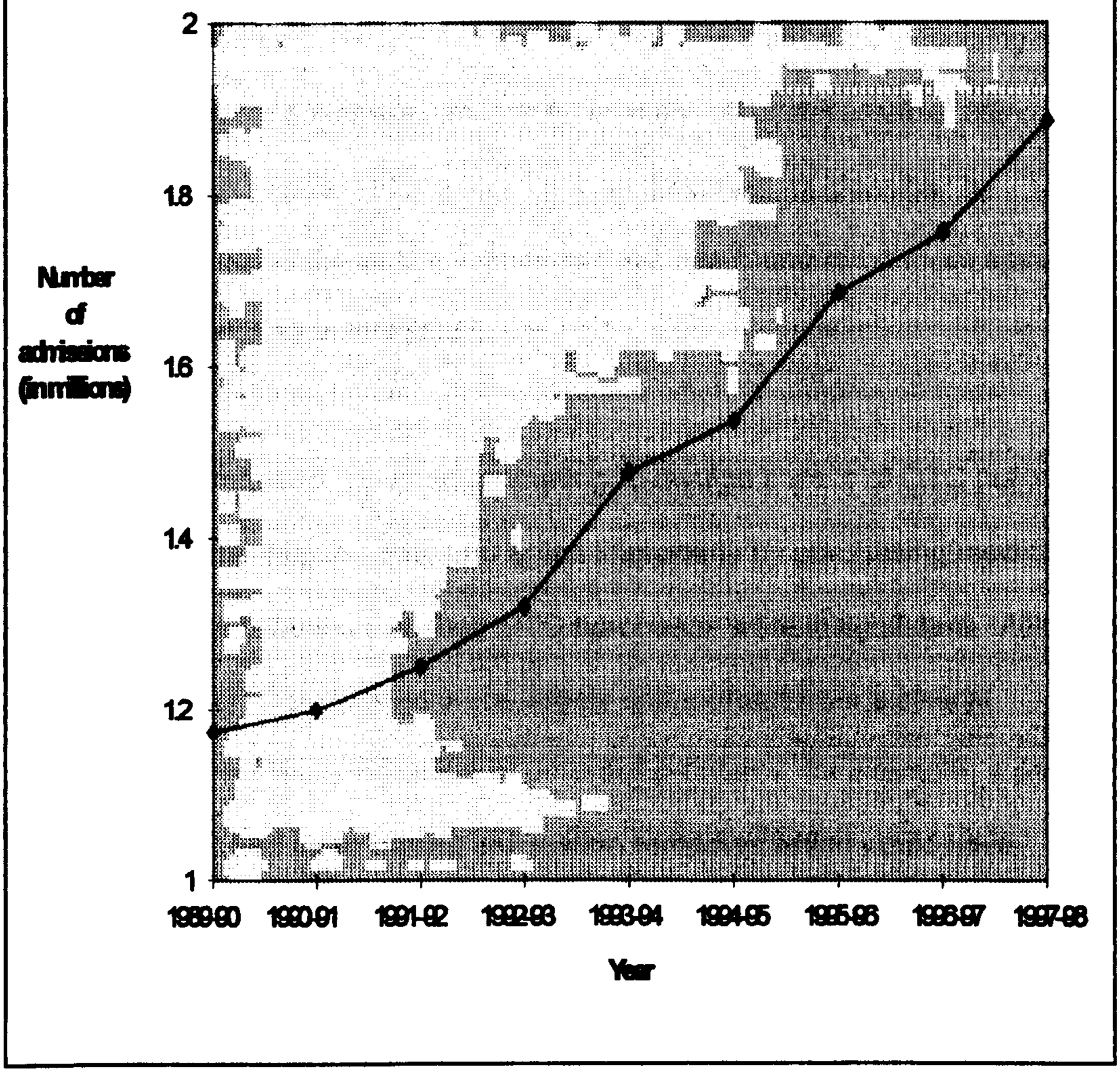
case). Important information about a significant number of hospital admissions that could be used to influence the management of patients prior to and following hospital discharge is not collected. As a result, the opportunity to educate prescribers and patients to improve drug use and reduce iatrogenic disease is lost. The drugs suspected of causing ADR related admissions, that is, diuretics, beta blockers and non-steroidal anti inflammatory drugs (NSAIDs), are similar to those reported by other workers[121] and are amongst the most commonly prescribed drugs in the UK. Recent work suggests that NSAID associated gastrointestinal bleeds are repsonsible for 2000 deaths a year in the UK.[122] Increasing awareness amongst prescribers of the common ADRs associated with these drugs and ensuring patients are aware of the potential problems with their medicines and action to take where appropriate could have a significant impact on this problem.

Studies have shown that many ADR related admissions are preventable; for example, one study found that 38.5% of ADRs thought to have caused hospital admission were either 'definitely' or 'possibly' avoidable.[123] It has also been demonstrated that a relationship to dosage and type (A or B) of ADR appeared to be strongly related to preventability.[124,125] It was demonstrated in these studies that 73-93% of ADRs are preventable. Inappropriate prescribing is responsible for a significant proportion of adverse drug reactions in the elderly.[81]

Despite evidence that many type A reactions are preventable and that a large proportion of ADR related hospital admissions are caused by a few classes of therapeutic agents, little action appears to have been undertaken to resolve the issue of ADRs and ADR related admissions resulting from the use of these

drugs. The number of total hospital admissions and general medical admissions is rising (Figure 11.3).

Figure 11.3 UK general medical admissions, 1989-1998



Since this research suggests the proportion of ADR related admissions has remained relatively constant, then, the absolute number of ADR-related admissions is rising. Methods of reducing the burden of ADR related admissions could include improved patient counselling, improved

communication between primary and secondary care and improving education about the signs and symptoms of ADRs, appropriate prescribing of drugs and improving recognition and reporting of ADRs.[123]

Causality assessment by the methods of Venulet and Ten Ham, which is based on a 'best fit' categorisation, was preferable to Naranjo's algorithm with the reports described here because of the flexibility that it afforded in judging some reactions. Reactions that were evidently 'unlikely' or 'unassessable' using Venulet and Ten Ham's method could still be classified as 'possible' by Naranjo's method, and thus the former method was found to be more applicable to reactions identified in this study.

Many patients required repeated prompting to divulge details of OTC purchases, possibly because they felt they had acted improperly by purchasing medicines or because they believed that their OTC purchases were insignificant. Although the majority of OTC purchases were largely unimportant from a clinical perspective others were indicative of potential problems: for example, a patient taking a NSAID had been buying indigestion remedies which could have indicated drug induced peptic ulcer disease; a second patient had been taking OTC ibuprofen and was found to be anaemic. A further concern was that 2 (6%) of the patients claiming drug allergies did not know to which drugs they were allergic. obtaining accurate drug histories from the majority of patients was often difficult and numerous patients were unsure of their exact drug therapy. Indeed on examination of patients' own medication which had been brought into the hospital, their medicine charts and relation to general practitioners records, irregularities were often identified. Again these deficiencies place patients at

risk from iatrogenic disease and at risk of omission of important medication.[126,127] A lack of reporting ADRs to the CSM / MCA and poor identification of ADRs suggests that a role for pharmacists in acute medical admissions and in monitoring patients for ADR related admissions exists.

11.6 Limitations.

This study presents data obtained from predominately elderly adult, medical patients at a large teaching hospital, in an area with socio-economic difficulties and who were not admitted directly to a specialist ward. Caution should be exercised in the extrapolation of these results to other populations including surgical or paediatric patients since previous work has demonstrated that the sample population may significantly influence the ADR related admission rate.[4] The high proportion of patients admitted with cardiovascular disease is indicative of the well described health problems endemic in the Liverpool area.[128] This may also influence the results of this study in comparison to an area with a lower incidence of coronary heart disease. The sample population was also of a relatively small sample size, although similar in size to some similar, published work.

Chapter 12:

Summary and conclusions

Chapter 12: Conclusions

12.1 ADR reporting schemes

Despite the evidence that in-house or local ADR reporting schemes can significantly increase ADR reporting rates within managed care institutions, few are in operation in UK hospitals. At present, the extent to which departments wish to involve themselves in the monitoring of ADRs remains the perogative of the units concerned. Where schemes are in operation, methods of reporting are reasonably similar. Few mechanisms for monitoring newly marketed agents exist in either local or national schemes and they do not appear to be particularly effective, given the number of reports received by them. Two years after the initial survey and a over a year after the introduction of ADR reporting for hospital pharmacists via the Yellow Card Scheme, few additional hospitals had developed systems for reporting ADRs. It is clear that neither the introduction of reporting for hospital pharmacists, nor the association between ADR reporting and clinical governance, have significantly encouraged units to develop schemes where previously none existed.

Previous estimates of the proportion of ADRs that remain unreported appear to high and somewhat over-optimistic based on the results of this work. While anecdotal evidence of commonly occurring or recognised ADRs is abundant, data which the CSM / MCA could need to take regulatory action if required, remain uncollected. ADR pharmacists appear to make a significant contribution to schemes in increasing rates of reporting, education and in operating the schemes themselves, and Drug Information pharmacists appear to have a similarly important role. Again, despite the demands of clinical governance and

improving quality in the NHS, few hospitals appear to have any systems in place for ensuring that ADRs are appropriately documented in patients' medical records and communicated to their primary health care providers (see below).

The work reported in this thesis demonstrates that education and training have a significant effect on pharmacists' participation in reporting via the Yellow Card Scheme and so it is disappointing that a significant number of departments have provided little or no education or training in this area.

12.2 Pharmacists' attitudes to and knowledge of ADR reporting

Pharmacists have a reasonable knowledge of the Yellow Card Scheme and consider it a professional obligation to participate in it. A lack of time appears to be a major obstacle to pharmacists reporting ADRs and this problem is likely to continue, given the current difficulties in staff recruitment and retention. Despite the majority knowing the criteria for reporting ADRs, many pharmacists are not prepared to report well recognised and minor reactions and pharmacists appear somewhat selective in the reactions they report in some instances, regardless of CSM criteria. The lack of leadership and encouragement concerning pharmacist ADR reporting from the RPSGB and the CSM / MCA has done little to remind pharmacists of the importance of postmarketing surveillance. Under reporting of ADRs remains a major problem.

As stated above, education and training provide a significant positive influence on participation in ADR reporting and knowledge of the scheme and this is a method by which reporting could be encouraged. The infrastructure for delivery

of postgraduate education is well established with the College of Pharmacy Practice and the Centre for Pharmacy Postgraduate Education continuing education schemes having key roles. It is worth noting that when reporting was first introduced for doctors and dentists, it took a number of years to reach the levels recorded in the late 1980's and early 1990's.[87] It is to be hoped that as the scheme continues, pharmacists will become more involved and that pharmacovigilance will become an integral part of their clinical activities.

12.3 Local scheme study

ADR reporting rates through the 'Green Card' Scheme at the RLUH have been substantially increased, although under-reporting at the hospital remains an issue. Analysis demonstrates the substantial contribution that pharmacists made to the scheme and identified areas which could be targeted to increase reporting. This was achieved through publicity, accessibility and the provision of feedback to reporters. With the advent of clinical governance and the wide uptake of its initiatives, local ADR schemes may become increasingly important for managed care institutions.

12.4 Transfer of ADR related data

GPs are dissatisfied with the current provision of information both in terms of quality and speed of transfer, which may have serious consequences for patient safety. Ensuring patients are aware of drugs to which they may be allergic or intolerant through verbal and written methods should minimise such risks. GPs were particularly concerned that they should receive information within an appropriate period of time following patients' discharge. Given the paucity of

methods of documenting and communicating this data (Chapters 4 and 5) a role for pharmacists exists, which could be supported by the use of a database such as HAROLD.

12.5 ADR related admissions

This study identified a numerically significant proportion of hospital admissions that were related to adverse drug reactions in line with previous studies. While the total number of acute medical admissions has increased, the proportion of patients admitted as a result of ADRs appears to have remained the same, despite a greater awareness of ADRs and issues of drug safety. This research suggests that the nature of drugs causing hospital admissions has not greatly altered, despite the fact that experience with the wide use of such drugs and that awareness of their adverse effects is widely publicised. Pharmacists should have a key role in monitoring patients for iatrogenic disease, collating details of such instances and providing feedback to prescribers to raise awareness of the problems associated with ADR related admissions.

12.6 Further research

Further scope exists for research into the role of pharmacists in ADR reporting. With the advent of computerised prescribing, the opportunities for obtaining details of ADRs electronically could revolutionise spontaneous ADR reporting. A number of hospitals in the UK now have such systems in operation and ADR reporting programmes should be built into their design and evaluated. Computer-based prescribing and ADR reporting combined would offer significant benefits over traditional spontaneous reporting, particularly for black

triangle drugs. Reporting would become faster and simpler and medication records could provide accurate and comprehensive drug histories. Local schemes could then begin to collect data which could be used to influence prescribing.

Issues surrounding ADR-related admissions require further research. Since they cause significant numbers of hospital admissions, further work is required to identify methods of predicting and preventing ADR related admissions. Larger studies would be required to achieve this.

12.7 Conclusion

This thesis has explored some of the issues affecting the role of the hospital pharmacist in pharmacovigilance. Local schemes have the potential to contribute greatly to pharmacovigilance but probably lack the attention and support they require to collect numbers of reports that reflect the number of ADRs that are occurring in hospitals should the results of published studies be generally applicable. This thesis has identified the level of hospital pharmacists and pharmacy departments' participation in local or in-house ADR reporting schemes. The factors identified as a result of the findings of this research can be used to influence the development of new schemes, or, to enhance existing schemes. Appropriate investment in these schemes needs to be encouraged in order to increase their effectiveness. Effective transfer of data is also important; this thesis demonstrates that in the Liverpool area at least, prescribers are dissatisfied with the manner and the timeliness of the information concerning ADRs they receive, if at all. This places patients and prescribers at risk from

inadvertent re-exposure to drugs suspected of previously causing an ADR. ADR related admissions remain a clinically and financially significant problem and strategies need to be developed to influence the reduction of their frequency. Education of both patients and prescribers is required to reduce this often preventable burden on the NHS.

Pharmacists have positive attitudes to the Yellow Card ADR reporting scheme and are aware of its importance and purpose; however, under reporting remains a substantial problem. Pharmacists lack confidence in the diagnosis of an ADR and appear to have taken a 'safety first' approach, that is, they tend to report well known, albeit serious, ADRs to the CSM / MCA. It is of concern that in the eighteen months following the introduction of ADR reporting for Pharmacists via the Yellow Card scheme, only a quarter of those able to report, have done so. The reasons for under-reporting described in this thesis and elsewhere[20,21] are in no way insurmountable. Like many aspects of clinical practice, education and training are the key initiatives required to enhance reporting of ADRs. The CSM / MCA also need to convince pharmacists that it is worth reporting ADRs that they suspect have occurred rather than ADRs they are certain have occurred. Department managers also need to attach more importance to the participation of their staff in ADR reporting by encouraging them.

A lack of leadership and encouragement mean that the CSM / MCA and the RPSGB need to take a more proactive approach and encourage potential reporters to actively participate in pharmacovigilance. If the maximum benefits from including pharmacists in the Yellow Card scheme are to be achieved then far greater investment is required in the promotion and publication of the

scheme to encourage potential reporters to participate. Pharmacists as the experts in medicines management have a challenging future as their role develops; however, it is important that in these new roles, the basic principles of pharmacovigilance and drug safety are not forgotten.

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Appendix 1:

Questionnaire and covering and follow up letters used in initial survey of hospital pharmacy departments

(Chapter 4)

Questionnaire to evaluate the role of the hospital pharmacist in adverse drug reaction monitoring.

1.0 About your Hospital

1.1) Approximately how many beds does your hospital have? Please circle.

0-400 401-800 801-1200 >1201

1.2) Is your hospital part of a larger NHS Trust? Y / N

If `No', please go to question 1.3.

If `Yes', approximately how many beds does your Trust have?

0-500 501-1000 1001-1500 >1500

1.3) Is your hospital affiliated to a university medical school? Y / N

1.4) Does your hospital have a clinical pharmacology department? Y / N

1.5) Does your hospital have a designated Adverse Drug Reaction Nurse? Y / N

2.0) About your pharmacy department

2.1) How many pharmacists are employed in your department? Please circle.

0-10 11-20 20-30 >30

2.2) Does your department have an designated drug information pharmacist? Y / N

2.3) Does your department have a designated drug information centre? Y / N

2.4) Does your department have an designated ADR specialist pharmacist Y / N

2.5) Do you operate a telephone help line for patients to ring in with drug queries? Y / N

If `No', please go to 2.6.

If `Yes', is the telephone help line used to identify and report ADRs? Y / N

2.6) Do you use an in house data collection form for gathering details (for example, patient details and examples of previous reports) of Adverse Drug Reactions that have been reported to pharmacy? Y / N

2.7) How do you decide to report ADRs via a `Yellow card' to the CSM? You may tick more than one.

a) Using an algorithm ☐

b) By discussion with a member of the medical staff ☐

c) Using your own clinical judgement ☐

d) Other, please elaborate.....

.....

2.8) Do you have any formal mechanisms for ensuring appropriate documentation of ADRs in the patients medical records? Y / N

If `No', please go to question 2.9.

If `Yes', please elaborate.....

.....

2.9) Do you have a formal mechanism for reporting ADRs to general practitioners? Y / N

If `No', please go to question 2.10.

If `Yes', please elaborate.....

.....

.....

2.10) Do you have a formal mechanism for reporting ADRs to community pharmacists? Y / N

If `No', please go to question 3.0.

If `Yes', please elaborate.....

.....

.....

3.0) Involvement in `Local' or `in house' reporting schemes.

3.1) Do you have a `Local' or `in house' adverse drug reaction (ADR) reporting scheme? Y / N

If `No', please go to question 4.1

3.2) If `Yes', and your hospital is part of a multi-centre NHS trust, does this scheme operate across all sites? Y / N

3.3) Who is responsible for the operation of the scheme? You may tick more than one category if operated by more than one discipline.

a) the pharmacy department ☐

b) the clinical pharmacology department ☐

c) other, please state.....

.....

3.4) How are ADR reports made. You may tick more than one.

a) by locally designed card sent to the pharmacy department ☐

b) by telephone to the pharmacy department ☐

c) other.....

.....

3.5) Who may report via your ADR reporting scheme? If `Anyone', please ignore other categories. Otherwise, you may tick more than one.

a) Anyone ☐

b) Doctors ☐

c) Nurses ☐

d) Pharmacists ☐

e) Patients ☐

f) Other, please elaborate.....

.....

3.6) Do you provide ADR reporters with feedback following their report?

Always / Never / On request only / For selected reports only

If `**Never**', please go to question 3.7.

Otherwise, which aspects of information concerning the ADR do you feed-back to the reporter?

a) An indication of the likelihood that the ADR was due to the suspect drug Y / N

b) An indication as to whether the ADR will be reported as a Yellow Card Y / N

c) An indication of the incidence of the ADR Y / N

d) Other, please elaborate.....

.....

3.7) Does your department publicise ADR monitoring within the hospital? Y / N

If `No', please go to question 3.8.

If `Yes', how is this achieved? You may circle more than one.

By ADR newsletter Y / N

By the Drugs and Therapeutics Committee newsletter Y / N

By promotion of the local scheme within the hospital Y / N

By posters on wards and in clinics Y / N

Other, please elaborate.....

.....

3.8) Do you keep a computer database of ADRs that have occurred in your hospital? Y / N

If `No', please go to question 3.9.

If `Yes', for what purposes do you use this database? Please elaborate.....

.....

.....

3.9) Do you have a particular system for reporting ADRs to new medicines (those marked with an inverted black triangle)? Y / N

If `No', please go to question 3.10.

If `Yes', how does this system for identifying ADRs to black triangle drugs operate? You may tick more than one.

a) By highlighting the drugs on prescription charts ☐

b) Pro-actively monitoring adverse effects of specific drugs ☐

c) Other.....

.....

3.10) Approximately how many ADR reports do you receive from the local reporting scheme each year? ☐

3.11) Approximately how many reports are forwarded to the CSM each as a result of this scheme each year? ☐

Now go to question 5.1

4.0 Pharmacy departments without a `local' or `in-house' ADR monitoring scheme.

4.1) Which issues do you consider to have prevented the operation of an ADR reporting scheme in your hospital? You may tick more than one.

a) Cost of the scheme ☐

b) Size of hospital ☐

c) A lack of perceived need to operate an ADR scheme ☐

d) Staffing ☐

e) Time ☐

f) Implementation of a scheme has never been considered ☐

g) Other, please elaborate.....

.....

4.2) Would you consider developing an ADR reporting scheme? Y / N

If `No' please go to question 4.3.

If `Yes', which type of scheme would you consider implementing within your hospital?

Please place in order of preference.

a) Locally designed ADR reporting card sent to the pharmacy department ☐

b) Reporting of ADRs by telephone to the pharmacy department ☐

c) Other.....

4.3) Do you participate in intervention monitoring as part of clinical pharmacy activities?

Y / N

If No, please go to question 4.4.

If Yes, do you collect data concerning Adverse Drug Reactions? Y / N

If No, please go to question 4.4.

If Yes, are `Yellow Cards' ever submitted to the Committee on Safety of Medicines as a result of these interventions? Y / N

4.4) Do you have a particular system for reporting ADRs to new medicines (those marked with an inverted black triangle)? Y / N

If `No', please go to question 5.1.

If `Yes', how does this system for identifying ADRs to black triangle drugs operate? You may tick more than one.

a) By highlighting the drugs on prescription charts ☐

b) Pro-actively monitoring adverse effects of specific drugs ☐

c) Other.....

.....

Thank you for completing the questionnaire. If you have designed cards or forms for reporting or collecting data, I would be extremely grateful to you if you could supply me with copies of the forms. Please feel at liberty to add any comments at the bottom of this sheet and overleaf.

0151-231-2066

Dear Colleague,

As a PhD research project, we are investigating adverse drug reactions in hospitals and the role of the pharmacist. A major part of our research is to evaluate the activities and degree of involvement of pharmacy departments in ADR monitoring and reporting throughout the United Kingdom.

I should therefore be grateful if you could assist us with this research project by completing the enclosed questionnaire. It is anticipated that it will take approximately ten minutes of your time and that virtually all questions may be answered without having to look up any data. Although the questionnaire may appear lengthy, the majority of questions are 'Yes / No' or 'Tick box' and not all questions need to be answered. Questionnaires maybe returned via the `FREEPOST' addressed envelope provided.

Please note that your responses will be treated with the utmost confidentiality and that questionnaires are coded purely to allow follow up of non-respondents. It would be greatly appreciated if you could return the questionnaire within the next two weeks.

We understand that your time is very precious, but your co-operation would be invaluable and greatly appreciated.

Thanking you in anticipation of your response.

Chris Green. BSc(Hons), Pgd. Dip.
Clin. Pharm, M.R.Pharm.S.

Prof. D. Mottram. B.Pharm,
PhD, F.R.Pharm.S

0151-231-2066

Dear Colleague,

Unfortunately, we do not appear to have received a response to the questionnaire we sent to you concerning your departments participation in adverse drug reaction monitoring. If you have already returned the enclosed questionnaire, please ignore this letter and accept our apologies.

If you have yet to return the questionnaire, we would be extremely grateful if you could do so. In order for our survey to be worthwhile, we need to reach a reasonable response rate which we have yet to do.

It is anticipated that it will take about five minutes of your time and that virtually all questions may be answered without having to look up any data. Although the questionnaire may appear lengthy, the majority of questions are 'Yes / No' or 'Tick box' and only about half of the questions need to be answered depending upon your responses. Questionnaires may be returned via the `FREEPOST' addressed envelope provided.

Please note that your responses will be treated with the utmost confidentiality and that they are coded purely to allow follow up of non-respondents. We understand that your time is very precious, but your co-operation would be invaluable and greatly appreciated, as without it our survey is of limited value.

Thanking you in anticipation of your response.

Chris Green. BSc(Hons), Pg. Dip. Clin.Pharm, MRPharmS.

Prof. D. Mottram. BPharm, PhD, FRPharmS.

Appendix 2:

Questionnaire and covering and follow up letters used in follow up survey of hospital pharmacy departments

(Chapter 5)

Adverse drug reaction monitoring: The role of hospital pharmacies

1.0 About your Hospital

1.1) How many in-patient beds does your hospital have? ☐

1.2) Is your hospital affiliated to a university medical school? Y / N

1.3) Does your hospital have a clinical pharmacology department? Y / N

1.4) Does your hospital have a designated Adverse Drug Reaction Nurse? Y / N

If **'Yes'**, what is the role of this nurse? .....

.....

.....

2.0) About your pharmacy department

2.1) How many full time equivalent pharmacists are employed in your hospital pharmacy department? ☐

2.2) Does your department have an designated drug information pharmacist? Y / N

2.3) Does your department have a designated drug information centre? Y / N

2.4) Do you operate a telephone help line for patients to contact with drug information queries? Y / N

If **'Yes'**, are ADRs identified using the help line, reported to the Committee on Safety of Medicines via the Yellow Card Scheme? Y / N

2.5) Does your department have an designated ADR specialist pharmacist? *Please circle one only.*

Full time / Part time / No

If **'Yes'** what is the role of this pharmacist?.....

.....

.....

Documentation and communication of ADR data

2.6) Do you use an in-house data collection form for gathering details of ADRs that have been reported to pharmacy *(for example, patient details and examples of previous reports)*? Y / N

2.7) Do you have any formal mechanisms for ensuring appropriate documentation of ADRs in patients medical records? Y / N

If `Yes', please elaborate.....

.....

2.8) Do you have a formal mechanism for reporting ADRs to general practitioners? Y / N

If `Yes', please elaborate.....

.....

2.9) Do you have a formal mechanism for reporting ADRs to community pharmacists? Y / N

If `Yes', please elaborate.....

.....

3.0) Involvement in 'Local' or 'in-house' reporting schemes.

3.1) Do you have a 'Local' or 'in-house' adverse drug reaction (ADR) reporting scheme? Y / N

If `No', please go to question 4.1

3.2) Who is responsible for the operation of the scheme? *You may tick more than one category if operated by more than one discipline.*

a) the pharmacy department ☐

b) the clinical pharmacology department ☐

c) Other, please state.....

3.3) How are ADR reports made. ***You may tick more than one.***

a) by locally designed card sent to the pharmacy department ☐

b) by telephone to the pharmacy department ☐

c) by CSM Yellow Card ☐

d) Other, please state.....

3.4a) Who may report via your ADR reporting scheme? ***Please tick as appropriate. If you tick 'Any member of staff', the other boxes may be left blank.***

a) Any member of staff ☐

b) Doctors ☐

c) Nurses ☐

d) Pharmacists ☐

e) Radiologists ☐

f) Other, please elaborate.....

3.4b) Can patients report an ADR via your local scheme? Y / N

3.5) Do you provide ADR reporters with feedback following their report? ***Please circle***

Always / Never / On request only / For selected reports only

3.6) How important is it to feedback to reporters within the local ADR scheme? ***Please circle.*** Very important / Important / Of little importance / Not important

3.7) Does your department publicise ADR monitoring within the hospital? Y / N

If 'Yes', how is this publicity achieved? ***You may tick more than one.***

a) By ADR newsletter ☐

b) By the Drugs and Therapeutics Committee newsletter ☐

c) Teaching sessions to doctors or nurses ☐

d) By posters on wards and in clinics ☐

e) Other, please elaborate.....

3.8) Do you keep a computer database of ADRs that have occurred in your hospital?

Y / N

If 'Yes', for what purposes do you use this database? Please elaborate.....

.....

.....

3.9) Who reviews ADR reports before submission to the CSM? ***Please tick one only.***

a) Pharmacists only ☐

b) A combination of pharmacists and medical staff ☐

c) Medical staff only ☐

d) Other(s), please state.....

3.10) What happens to a local ADR report in order for it to be processed and sent to the CSM as a Yellow Card report? Please state.....

.....

3.11) Approximately how many ADR reports do you receive from the local reporting scheme each year? ☐

3.12) Approximately how many reports are forwarded to the CSM each as a result of this scheme each year? ☐

3.13 Please use the space below to comment on your particular scheme. Please comment on anything that might make your scheme particularly novel or unique.

.....

.....

.....

.....

Now go to section 5.0

4.0 Pharmacy departments without a 'local' or 'in-house' ADR monitoring scheme.

4.1) Will you be developing an ADR reporting scheme? *Please tick the appropriate answer.*

a) We have definite plans to introduce an ADR reporting scheme ☐

b) We have probable plans to introduce an ADR reporting scheme ☐

c) We have no intention of introducing an ADR reporting scheme ☐

Please continue to section 5.0

5.0 Monitoring newly marketed agents

5.1) Do you have a particular system for reporting ADRs to new medicines (those marked with an inverted black triangle)? Y / N

If 'Yes', how does this system for identifying ADRs to black triangle drugs operate? *You may tick more than one answer.*

a) By highlighting the drugs on prescription charts ☐

b) By highlighting the containers of newly marketed drugs ☐

c) Other (please state).....

.....

6.0 Education and training.

6.1) Has your department held any training or education meetings to discuss ADR reporting since the introduction of Yellow Card reporting for pharmacists?

Y / N

If 'Yes' what has this involved? *You may tick more than one.*

a) Workshop / discussion sessions ☐

b) Distribution of CSM information pack ☐

c) Formal lectures ☐

d) Initiation of local schemes and issues relating to implementation ☐

e) Other, please state.....

.....

.....

Thank you for completing the questionnaire. If you use locally designed cards, I would be extremely grateful to you if you could supply me with a copy for the purpose of comparison. Please feel at liberty to add any comments at the bottom of this sheet and overleaf.

0151-231-2066

Dear Colleague,

As a PhD research project, we are investigating adverse drug reactions in hospitals and the role of the pharmacist. A major part of our research is to evaluate the activities and degree of involvement of pharmacy departments in ADR monitoring and reporting throughout the United Kingdom. You may remember that we sent you a questionnaire in August 1996. As a result of our findings we were able to publish a paper in the International Journal of Pharmacy Practice and present a summary of our finding as at the United Kingdom Clinical Pharmacy Association Symposium. However, we have been asked and are interested to discover whether the introduction of Yellow Card reporting for pharmacists has been affected the number of departments operating local schemes.

I should therefore be grateful if you could assist us with this research project by completing the enclosed questionnaire. It is very similar to the previous questionnaire and it anticipated that it will take approximately five minutes of your time and that virtually all questions may be answered without having to look up any data. Although the questionnaire may appear lengthy, the majority of questions are `Yes / No' or `Tick box' and not all questions need to be answered. Questionnaires maybe returned via the `FREEPOST' addressed envelope provided.

Please note that your responses will be treated with the utmost confidentiality and that questionnaires are coded purely to allow follow up of non-respondents. It would be greatly appreciated if you could return the questionnaire within the next two weeks.

We understand that your time is very precious, but again, your co-operation would be invaluable and greatly appreciated.

Thanking you in anticipation of your response.

Chris Green. BSc(Hons), Pgd. Dip.
Clin. Pharm. M.R.Pharm.S.

Prof. D. Mottram. B.Pharm
PhD, F.R.Pharm.S

15th August 1998

Dear colleague,

Re: Questionnaires and adverse drug reaction reporting

Unfortunately, we do not appear to have received a response to the questionnaire we sent you concerning your department's involvement in ADR monitoring and related activities. If you have already returned the questionnaire, please do so and accept our apologies.

If you have yet to return the questionnaire, we would be extremely grateful if you could do so. As this is a follow up study,[1] we need to attain a similar response rate to that of our previous survey. Unfortunately, we are currently some way short of this target at the moment.

We should therefore be grateful if you could, once again, assist us with this research project by completing the enclosed questionnaire. It is anticipated that it will take approximately five minutes of your time as virtually all questions may be answered without having to look up any data. Although the questionnaire may appear lengthy, the majority of questions are `Yes / No' or `tick box' and not all questions need to be answered. Questionnaires may be returned anonymously via the `FREEPOST' addressed envelope provided and it would be greatly appreciated if you could do so within the next two weeks.

We understand that your time is very precious but again, your co-operation would be invaluable and greatly appreciated, as without it, our survey is of limited value.

Thanking you in anticipation of your response.

Chris Green. BSc(Hons), Pgd. Dip. Clin. Pharm. M.R.Pharm.S.

Prof. D. Mottram. B.Pharm, PhD, F.R.Pharm.S

1. Green CF, Mottram DR, Rowe P, Brown AM. An investigation into adverse drug reaction monitoring by United Kingdom Hospital pharmacy departments. International Journal of Pharmacy Practice. 1997; 5: 202-208.

N.B. If you would like a copy of the article in the International Journal Of Pharmacy Practice, please fill in the form and return it either with the questionnaire or separately to the same address using the FREEPOST address below.

Name .....

Job Title .....

Hospital .....

Hospital Address .....

.....

Chris Green
c/o School of Pharmacy and Chemistry
Liverpool
70 Great Crosshall St
Liverpool
FREEPOST
L3 5UY

Appendix 3:

Questionnaire guide used in qualitative interviews with hospital pharmacists (Chapter 6)

Hospital pharmacists and ADR reporting

How many years have you been qualified?

Postgraduate qualifications?

Speciality?

So you're aware that you can report ADRs via the Yellow Card scheme?

Have you participated in any education or training with regard to the introduction of ADR reporting for pharmacists?

Did you find that encouraged you to participate in ADR reporting?

Do you think you're trained in such a way that you go out and look for ADRs?

What do you think about the introduction of ADR reporting for pharmacists?

What was your reaction personally when you discovered you could report ADRs via the Yellow Card scheme?

How prepared did you feel prepared to participate in the scheme when pharmacists were officially involved in the scheme?

How many ADRs have you reported since the introduction of pharmacist reporting?

What made the ones you reported stand out?

What concerns do you have about ADR reporting, for example, confidence, appropriateness, time, role, legal angle?

As for reasons why you might not report an ADR, would a lack of time prevent you from reporting ADRs?

What about motivation?

What about a lack of information about a patient?

What about your' clinical knowledge or lack of diagnostic ability as a pharmacist?

Would the fact that a suspected reaction was unusual or bizarre stop you reporting it?

Does patient confidentiality concern you?

Are there any other reasons for under reporting that I haven't raised?

What's the one thing that you would say is deterring you from reporting ADRs?

Obviously the CSM co-ordinates the Yellow Card scheme, how does CSM Mersey fit into this ?

Have you ever contacted CSM Mersey or had any dealings with them?

Why / not?

What was your impression?

What else could they do for you or to encourage you to report?

Did you receive the information pack (show pack) regarding ADR reporting from the MCA/CSM?

What did you think of the information pack?

What do think about current problems?

The CSM resisted introducing reporting for pharmacists and it was widely reported in the PJ. Do you have any views on the adverse publicity generated by the CSM concerning ADR reporting for pharmacists?

What do you think about a fee for reporting ADRs?

The CSM have published criteria concerning what should be reported to them via the Yellow Card scheme. What do you think about them? ***(show copy)***

Pharmacists have to report ADRs using a separate form. Do you have any thoughts about this?

Are you conscious that when you report something that you're reporting as a pharmacist and are you worried about what the CSM might think of your reports?

Do you have any thoughts about the structure of the Yellow Card in general or how might it be improved?

How certain do you think you need to be before reporting an ADR?

Would you report a reaction you were merely suspicious of being an ADR?

What would constitute a reaction you would consider worthy of reporting to the CSM?

What do you think about the BTD scheme?

Would you report minor reactions like nausea, rash or cough with a black triangle drug?

If any, what sort of feedback would you like from the CSM?

If they wrote back to you and said thanks for your report but we didn't feel it was an ADR. How would you feel about that, would it dissuade you from reporting another ADR or would it not?

Do you have any concerns about a copy of your report going to the patients doctor?

Have you contacted any pharmaceutical companies for information about ADRs? Describe your experiences and thoughts about them.

Does the follow up they send deter you from calling them?

Do you see ADR reporting is a professional obligation?

A doctor tells you not to report an ADR you are convinced should be reported, would you? Why?

What has your department done to encourage your participation in ADR reporting? What could they do?

What else might encourage you to report ADRs?

What about an element of competition?

Does your hospital have a local ADR reporting scheme or procedure? What do you think about this?

Finally, do you have any final or overall thoughts about ADR reporting for pharmacists? What about the Yellow Card scheme? Is there any thing that we have not covered in the questionnaire that you would like to discuss?

Appendix 4:

Questionnaire used in postal questionnaire survey of hospital pharmacists

(Chapter 7)

The Yellow Card Scheme and the Hospital Pharmacist

Section 1: The Yellow Card Scheme and pharmacovigilance

1. Are you aware that as a hospital pharmacist you can report adverse drug reactions (ADRs) to the Committee on Safety Of Medicines (CSM) via the Yellow Card ADR reporting scheme? **Please tick**

Yes ☐ No ☐

If **'Yes'** what alerted you to the fact that as a hospital pharmacist you could report ADRs via the Yellow Card scheme? ***You may tick more than 1 answer.***

Pharmaceutical Journal articles ☐

Departmental meeting or announcement ☐

Discussion with colleagues ☐

I received a copy of the CSM information pack "Pharmacovigilance: The Yellow Card Scheme: Information Pack For Pharmacists" ☐

Other (please specify)_____

---

2. Did you consider yourself adequately informed about the national launch of Yellow Card reporting for pharmacists? **Please tick**

Yes ☐ No ☐ Can't remember ☐

3. Have you reported an ADR to the Committee on Safety of Medicines (CSM) (either directly or as part of a local ADR scheme) since April 1997? **Please tick**

Yes ☐ No ☐

If 'Yes', how many reactions have you reported? ☐

4. What do understand by the inverted black triangle (▼) placed next to medicines?

5. Which reports does the CSM wish to receive? ***Please tick the appropriate answer for each statement.***

a) For newly marketed (black triangle) agents

All reactions ☐ *Serious reactions only* ☐ *No reactions* ☐ *Don't know* ☐

b) For established products

All reactions ☐ *Serious reactions only* ☐ *No reactions* ☐ *Don't know* ☐

c) For vaccines

All reactions ☐ *Serious reactions only* ☐ *No reactions* ☐ *Don't know* ☐

d) For herbal drugs

All reactions ☐ *Serious reactions only* ☐ *No reactions* ☐ *Don't know* ☐

e) Only proven ADRs

True ☐ *False* ☐ *Don't know* ☐

6. What is the purpose of the Yellow Card ADR reporting scheme? ***Please tick the appropriate answer for each statement.***

To enable safe drugs to be identified	Yes ☐	No ☐	Unsure ☐
To measure the incidence of ADRs	Yes ☐	No ☐	Unsure ☐
To identify factors that might predispose patients to ADRs	Yes ☐	No ☐	Unsure ☐
To identify previously unrecognised ADRs	Yes ☐	No ☐	Unsure ☐
To obtain information about the characteristics of particular reactions	Yes ☐	No ☐	Unsure ☐
To compare adverse effects of drugs within the same therapeutic class	Yes ☐	No ☐	Unsure ☐

7. Please state whether you agree or disagree with the following statements about ADR reporting. **Please tick the appropriate answer for each statement.**

ADR reporting is a professional obligation for pharmacists.

Agree ☐ Disagree ☐ No opinion ☐

One ADR report makes no difference to the Yellow card scheme.

Agree ☐ Disagree ☐ No opinion ☐

All serious ADRs are identified by the time a drug is marketed.

Agree ☐ Disagree ☐ No opinion ☐

Yellow cards are too complicated to fill in

Agree ☐ Disagree ☐ No opinion ☐

It is adequately clear to me what I should and should not report to the CSM.

Agree ☐ Disagree ☐ No opinion ☐

8. Have you ever contacted a pharmaceutical manufacturer with regard to a suspected ADR? **Please tick.**

Yes ☐ No ☐

If 'Yes', did the company send you forms or documents to be completed with regard to the suspected ADR? **Please tick.**

Yes ☐ No ☐

If 'Yes' did this request for follow up deter you from contacting them for information again? **Please tick.**

Yes ☐ No ☐

9. In your opinion should ADR reporting via the CSM/ MCA Yellow Card scheme be compulsory or voluntary?

Compulsory ☐ Voluntary ☐ No opinion ☐

10. Since April 1997, have you had patient contact as part of your job? **Please tick**

Yes ☐ No ☐

If 'No' go to 'Section 3'

Section 2: Reporting adverse drug reactions

11. Which of the following factors would encourage you to report an ADR? **Please tick the appropriate answer for each statement.**

The reaction is of a serious nature — Yes ☐ No ☐

The reaction is unusual — Yes ☐ No ☐

The reaction is to a new product — Yes ☐ No ☐

Certainty that the reaction is a true ADR — Yes ☐ No ☐

The reaction is a well recognised for a particular agent — Yes ☐ No ☐

12. Have you at any time since April 1997 **not reported** an ADR knowing that a doctor would be reporting the reaction themselves? **Please tick.**

Yes ☐ No ☐ Situation has never arisen ☐

13. Have you at any time since April 1997 prepared or completed a Yellow Card for a doctor to sign? **Please tick**

Yes ☐ No ☐ Situation has never arisen ☐

14. Have you ever used information obtained from the CSM, i.e. numbers or details of previous reports, to assist you in the evaluation of a potential adverse drug reaction?

Yes ☐ No ☐

15. Do you have access to CSM information in your department either in microfiche or CD ROM format ?

Yes ☐ No ☐ Don't know ☐

16. Are you aware that the patient's consultant receives a copy of Yellow Card reports you send to the CSM?

Yes ☐ No ☐

17. Which of the following factors might discourage you from reporting an ADR?
You may tick more than 1 answer.

Concern that a doctor gets a copy of my Yellow Card report	☐
Lack of confidence in discussing a potential ADR with the prescriber	☐
Apprehension about sending in an inappropriate report	☐
Lack of time to fill in a report	☐
Concern that a report would generate follow up from the CSM resulting in extra work	☐
The absence of a fee for reporting ADRs	☐
Lack of time to actively look for ADRs while in clinical practice	☐
Level of clinical knowledge makes it difficult to decide whether or not an ADR has occurred.	☐
Don't feel the need to report well recognised reactions	☐
Pharmacist yellow card report forms not available when needed	☐

18. For the following examples, please indicate whether you would report an ADR via the Yellow Card scheme. Assume that each symptom is likely to have been caused by the suspect drug. **Please tick the appropriate answer for each statement.**

Jaundice with frusemide	Yes	☐	No	☐	Don't Know	☐
Headache with venlafaxine	Yes	☐	No	☐	Don't Know	☐
Cold extremities with β blockers	Yes	☐	No	☐	Don't Know	☐
Thrombocytopenia with heparin	Yes	☐	No	☐	Don't Know	☐
Nausea with montelukast	Yes	☐	No	☐	Don't Know	☐
Gastrointestinal bleed with diclofenac	Yes	☐	No	☐	Don't Know	☐

19. Have you received specific training about ADRs? ***Please tick.***

Yes ☐ No ☐

If 'Yes', what is the nature of the training you received? ***Please tick***

Departmental meeting Yes ☐ No ☐

Local RPSGB branch meeting Yes ☐ No ☐

CSM study day / study evening Yes ☐ No ☐

Other_____ Yes ☐ No ☐

20. How could reporting of ADRs by hospital pharmacists be improved or made easier?

21. Where would you obtain information concerning ADRs or ADR reporting?

Section 3: For the purposes of demographical and statistical analysis, please complete the following section about yourself.

22. Job title ☐

23. Age ☐

24. Are you retired? Yes ☐ No ☐

25. Please state the number of years you have been qualified ☐

26. How many of these have been spent in hospital practice? ☐

27. Is the area in which you practice part of a CSM regional monitoring centre (i.e. CSM Mersey, Wales, Midlands or Northern)?

Yes ☐ No ☐ Don't know ☐

Thank you for completing this questionnaire, please feel free to add any further comments or observations below or on the reverse side of this page.

0151-231-2066

Dear Colleague,

Re: Hospital Pharmacists and their new role in ADR reporting

As a PhD research project, we are investigating the role of hospital pharmacists in adverse drug reaction monitoring, particularly with regard to the Yellow Card scheme. We should therefore be grateful if you could complete the enclosed questionnaire.

Although the questionnaire may appear lengthy, virtually all questions are 'tick box' and it is anticipated that it will take approximately five minutes to complete. The completed questionnaire may be returned anonymously via the 'FREEPOST' addressed envelope provided. As this is a key component of our research, it would be greatly appreciated if you would return the questionnaire within the next two weeks.

Thanking you in anticipation of your response.

Chris Green. BSc (Hons), Pgd. Dip. Clin. Pharm. M.R.Pharm.S.

Prof. D. Mottram. B.Pharm, PhD, F.R.Pharm.S

0151-231-2066

Dear Colleague,

Re: Hospital Pharmacists and their new role in ADR reporting.

We recently sent you a copy of the enclosed questionnaire concerning hospital pharmacists' involvement in adverse drug reaction monitoring. Unfortunately, the initial distribution of this questionnaire resulted in lower return rate than we had hoped for. In order to gain a meaningful response rate, it is necessary to distribute the questionnaire a second time. If you have already completed and returned a copy of this questionnaire, please ignore this letter and we apologise for the inconvenience caused.

Although the questionnaire may appear lengthy, virtually all questions are 'tick box' and it is anticipated that it will take approximately five minutes to complete. The completed questionnaire may be returned anonymously via the 'FREEPOST' addressed envelope provided. As this is a key component of our research, it would be greatly appreciated if you would return the questionnaire within the next few weeks.

Thanking you in anticipation of your response,

Yours sincerely,

Chris Green. BSc (Hons), Pgd. Dip. Clin. Pharm. M.R.Pharm.S.

Prof. D. Mottram. B.Pharm, PhD, F.R.Pharm.S

Appendix 5:

Data collection forms and assessment criteria used in the local ADR reporting scheme (Chapter 9 and Chapter 11)

Causality assessment

From: Venulet J. Ten Ham M. Methods for monitoring and documenting adverse drug reactions. Int. J. Clin. Pharmacol. Ther. 1996; 34 (3):112-129.

Certain. A clinical event, including laboratory test abnormality, occurring in a plausible time relationship to drug administration and which cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the drug (dechallenge) should be clinically plausible. The event must be definitive pharmacologically or phenomenologically, using a satisfactory rechallenge procedure if necessary.

Probable / likely. A clinical event, including laboratory test abnormality, with a reasonable time sequence to administration of the drug, unlikely to be attributed to concurrent disease or other drugs or chemicals, and which follows a clinically reasonable response on withdrawal (dechallenge). Rechallenge information is not required to fulfil this definition.

Possible. A clinical event, including laboratory test abnormality, with a reasonable time sequence to administration of the drug but which could also be explained by concurrent disease or other drugs or chemicals. Information on drug withdrawal may be lacking or unclear.

Unlikely. A clinical event, including laboratory test abnormality, with a temporal relationship to drug administration which makes a causal relationship improbable and in which other drugs, chemicals or disease provide plausible explanation.

Conditional / unclassified A clinical event including laboratory test abnormality, reported as an adverse drug reaction about which more data is essential for a proper assessment or the additional data are under examination

Unassessable / unclassified A report suggesting an adverse drug reaction which cannot be judged because information is insufficient or contradictory and which cannot be supplemented or verified.

Severity assessment

Following CSM guidelines, 'Serious' reactions include those that are fatal, life threatening, disabling, incapacitating or which result in or prolong hospitalisation. The remainder are classified as 'Non serious'. N.B. All reactions should be reported for black triangle drugs▼.

PAGE/PAGES
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UNDER
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FROM
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ADR Investigation Form

Patient's name / unit number
or Adressograph:

Ward / Clinic.....

Consultant.....

Age yrs Weight kg Male / Female Pregnant Y / N

Relevant medical history

Reason for admission Date / /

.....

.....

.....

Other diagnoses	Chronic / Acute (C / A)	Dates / Duration

DRUG THERAPY - see attached sheet

OTC / Herbal / Other.....

ALLERGIES
(Drugs or otherwise) Y / N / NK
Details.....

Lab data sheet attached? Y / N

.....

Renal function Normal / Impaired / Unknown

Hepatic function Normal / Impaired / Unknown

Adverse event details

Date of onset / /

Time after suspect drug.....

Duration of adverse event .....

Time after admission.....

Description.....

.....

.....

.....

.....

Severity (Circle): Fatal / Serious / Moderate / Mild / Unclassifiable

Type A or B A / B

Was hospital admission due to ADR? Y / N

Treatment

Suspect drug withdrawn Y / N / Stat dose

Dose reduced Y / N / NA If 'Yes' state new dose.....

Was drug therapy altered? Y / N / NA

Was corrective treatment prescribed? Y / N / NA

If 'Yes' give details: Drug.....
Dose.....
Indication.....
Duration.....

Did symptoms resolve? Y / N

Was hospital stay prolonged? Y / N / NA / OPD

Comment.....

Outcome Full recovery / Almost resolved / No change / Worse / Fatal

NON DRUG CAUSES:- Ask opinion of experienced doctor.

Could the patients medical condition have caused the event?

Almost definitely / Probably / Possibly / Unlikely / Unknown

Yellow Card Report appropriate? Y / N

ADR investigation form - patients drugs

Drug	Dosage form	Dose	Route	Freq.	(Y / N)	Start date	Stop date	Indication

Appendix 6:

Questionnaire used in postal questionnaire survey of general practitioners

(Chapter 10)

Adverse Drug Reactions experienced by hospital in-patients. An evaluation of the provision of information to general practitioners and their patients.

Part 1. Current provision of information

1.1) How often do you see patients who have experienced an adverse drug reaction while a hospital in-patient?

Never / Rarely / Occasionally / Frequently

If 'Never' please got to question 1.6, otherwise please continue

1.2) How often has a patient told you that they experienced an ADR whilst in hospital but there is no record of this in their discharge documentation. Please circle.

Never / Rarely / Occasionally / Frequently

If 'Never' please got to question 1.6, otherwise please continue

1.3) How often can these patients name the exact drug suspected of causing the ADR?

Never / Rarely / Occasionally / Frequently

1.4) How often can these patients describe the exact nature of the reaction?

Never / Rarely / Occasionally / Frequently

1.5) How confident are you in the information patients give you?

Very confident / Confident / Uncertain / Very uncertain

1.6) Where ADRs are reported in the discharge documentation, how frequently is the information available sufficient to make an informed opinion concerning a patients ADR?

Never / Rarely / Occasionally / Frequently

1.7) How frequently is the combined information available from the patient and the discharge documentation sufficient to make an informed opinion concerning a patients ADR?

Never / Rarely / Occasionally / Frequently

1.8) How could hospitals improve the communication of ADR data to general practitioners? Please comment.

Part 2: ADR notification form.

Attached, is a sample of a standard form we intend to send to general practitioners who's patients have experienced an ADR at the RL&BUHT.

2.1) What additional information would you like to receive? Please state.

2.2) What information included in the form is unnecessary? Please state

2.3) Should patients receive a copy of this notification form?

Yes / No

Please give reasons for your answer.

2.4) It is proposed to supply patients with a 'credit card' sized ADR warning card naming the drug(s) suspected of causing an ADR. Do you consider this to be a useful idea?

Yes / No

Please comment if you wish.

2.5) If introduced, should this card include a description of the ADR experienced by the patient?

Yes / No

Please comment if you wish.

2.6) How would you prefer to receive information about ADRs, please tick *one* only.

As part of the discharge documentation ☐
As a separate notification form ☐

Other, please state.....

Thank you for completing this questionnaire. Please feel free to add any further comments below or overleaf.

Sample ADR Notification Form

A GP
The Surgery
A Road
A Town

Dear Doctor,

I am writing to inform you of a suspected adverse drug reaction experienced by one of your patients. Details of the patient concerned and the nature of the suspected reaction are listed below.

Patient Name: A Patient

Date of Birth: DOB

Patient address: A road, A town

Unit Number: 12345678S

Consultant: A Doctor

Suspect Drug: A drug

Details of ADR: Details of reaction including details of abnormal laboratory data.

Additional information: This section will be used for further information when needed.

A 'Yellow Card' report of this reaction was / was not sent to the CSM.

Additional information is available from the pharmacy department at the Royal Liverpool Hospital. For further or related information, please telephone 706-2096. Please quote the ADR number when calling.

Yours sincerely,

AN Other.

Pharmacy Department
Ext. 2135

Dear Doctor,

Re: Adverse Drug Reactions - announcement of a new ADR notification scheme.

At the Royal Liverpool and Broadgreen University Hospitals, we are aiming to improve our documentation and communication of data relating to adverse drug reactions.

Enclosed is a form that we propose to use to notify general practitioners of ADRs experienced by their patients. As the form is intended to provide you with information, it is vital that we receive your comments concerning its content.

We would therefore be grateful if you could review the sample notification form enclosed, complete the short questionnaire and return it to us at the RL&BUHT using the envelope provided. The majority of questions are 'circle' or 'tick box' in design and the questionnaire is designed to be completed in a few minutes.

Yours sincerely,

Chris Green
ADR research pharmacist.

Solomon Almond
Senior Registrar,
Clinical Pharmacology.

Pharmacy Department
Ext. 2135

Dear Doctor,

Re: Adverse Drug Reactions - announcement of a new ADR notification scheme.

We recently sent you a copy of the enclosed questionnaire concerning the communication of data concerning adverse drug reactions. Unfortunately, the initial distribution of this questionnaire resulted in lower return rate than we had hoped for. In order to gain a meaningful response rate, it is necessary to distribute the questionnaire a second time. If you have already completed and returned a copy of this questionnaire, please ignore this letter and we apologise for the inconvenience caused.

At the Royal Liverpool and Broadgreen University Hospitals, we are aiming to improve our documentation and communication of data relating to adverse drug reactions. Enclosed is a form that we propose to use to notify general practitioners of ADRs experienced by their patients. As the form is intended to provide you with information, it is vital that we receive your comments concerning its content.

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Yours sincerely,

Chris Green
ADR research pharmacist.

Solomon Almond
Senior Registrar,
Clinical Pharmacology.

Appendix 7:

CSM / MCA Yellow Card

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Appendix 8:

Publications associated with this thesis.

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