A Study of Multiple Perspectives and Knowledge in Adverse Drug Reaction Decision-making

Volume 1

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Abstract

Injury and illness associated with drugs are major problems in Australia and around the world, despite significant developments in the area of adverse drug reaction (ADR) decision support technology. The aims of this thesis are: to investigate the ADR decision domain; to determine factors that may assist in the prevention, detection and management of ADRs; and, to inform the pre-requirements analysis phase of the development of decision support systems.

An approach has been taken that permits open and grounded study of the decision environment. This approach can then be used to frame and inform the design of an ADR decision support system.

Fifteen case studies that comprise self selected consumers, the treating medical practitioner/s and expert perspectives of a single instance of an ADR (fifteen in-depth consumer interviews, eight in-depth medical practitioner interviews and 30 expert written questionnaires), have been collected and analysed using a grounded theory approach, a symbolic interactionist theoretical framework and a social constructionist epistemology. The analysis was performed from three perspectives: individual case study analysis (all interviews for an instance of an ADR); group analysis (consumer, medical practitioner and expert views) and analysis combining the individual case studies and groups of data.

Concepts, themes and theory have emerged from these data in the following areas:

- the contribution of the differences in understanding of the core concepts within this domain, to misunderstandings between decision-makers;
- the consumer as a diagnostic decision-maker in the ADR decision domain;
- differential diagnostic strategies used by the consumers and medical practitioners;
- complexities in the ADR decision domain that make diagnosis difficult;
- the role of ADR information in consumer and medical practitioner decision-making;

- decision types used by consumers and medical practitioners in the ADR decision domain;
- resources used by consumers, medical practitioners and experts to inform their ADR decisions;
- decision-making with partial knowledge of the consumer case history, drug behaviour and diseases;
- the impact of suspected ADRs on consumers and on future decision-making;
- medical practitioner/consumer decision-making models; and,
- reasons for low ADR reporting and the impact on the development of new ADR knowledge.

The results above suggest the following:

- The ADR decision domain is more complex than the current ADR decision support focus and that broadening this focus may assist in providing a more complete and useful decision support solution.
- Improving the prevention, detection and management of ADRs requires more than providing prescribers with up to date ADR information. Other important factors are sharing of information, awareness of the role of the consumer, a collaborative approach between the consumers and medical practitioners, and generation of new ADR knowledge.
- A grounded theory analysis of case study data using the theoretical perspectives of social constructionism and symbolic interactionism provided insight into this domain from the perspectives of multiple decision-makers. This may be an approach that can be used by systems analysts to inform the requirements analysis phases of decision support within other domains.

The results of this qualitative work are preliminary. Future work is required to confirm and expand these results.

Statement of Authorship

Except where explicit reference is made in the text of the thesis, this thesis contains no material published elsewhere or extracted in whole or in part from a thesis by which I have qualified for or been awarded another degree or diploma. No other person's work has been relied upon or used without due acknowledgement in the main text and bibliography of the thesis.

The following publications and reports have resulted from the work of this thesis:

O'Brien, M. C. (2001). *Final report to department of health and aged care for contract for services GPCG #12. Adverse drug reactions improved decision support (ADRIDS)*. Ballarat: Collaborative Centre for E-Health.

O'Brien, M. C., & Yearwood, J. L. (2002). *Insights into consumer/doctor decisions surrounding adverse drug reactions and prescribing*. University of Ballarat.

O'Brien, M. C., & Yearwood, J. L. (2003). *Insights into consumer decisions surrounding adverse drug reactions: Some preliminary results*. Paper presented at the Combined Conferences of the Eleventh National Health Informatics Conference, Applying Socio-technical Practices and Principles, and the Twelfth National RACGP Computer Conference, Beyond the Box: Making IT work for GP's and Patients., Sydney, Australia.

O'Brien, M. C., & Yearwood, J. L. (2004). *Risk: Drug therapy versus adverse drug reaction. A case study approach with consumer, medical and expert views*. Paper presented at the 12th Health Informatics Conference: Let's Make a Difference with Health ICT, Brisbane, Australia.

O'Brien, M. C. & Yearwood, J. L. (2005). Decisions Surrounding Adverse Drug Reaction Prescribing: Insights from Consumers and Implications for Decision Support. *Journal of Research and Practice in Information Technology, 37*(1), 57-71.

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Statement of Ethics Approval

This research was approved by the following ethics committees:

- University of Ballarat Human Research Ethics Committee;
- Ballarat Health Services and St. John of God Health Services, Combined Hospitals Ethics Committee.

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This thesis is dedicated to Emily.

May you find your own path to knowledge.

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List of Abbreviations

ADE	Adverse Drug Event
AE	Adverse Event
ADR	Adverse Drug Reaction
ADRAC	Adverse Drug Reaction Advisory Committee
ADRIDS	Adverse Drug Reaction Improved Decision Support
BDDGP	Ballarat and District Division of General Practitioners
CMI	Consumer Medicine Information
CRM	Consumer Report on Medicines
DSS	Decision Support System
EDDS	Electronic Decision Support Systems
EUT	Expected Utility Theory
GP	General Practitioner
GPCG	General Practitioner Computer Group
HIC	Health Insurance Commission
ICTSC	Information and Communication Technology Standards Committee
IS	Information Systems
ISA	Intelligent Software Agent
MAS	Multi-Agent Systems
MAUT	Multi-Attribute Utility Theory
MSIA	Medical Software Industry of Australia
NHIMAC	National Health Information Management Advisory Council
NICS	National Institute of Clinical Studies
NPS	National Prescribing Service
PI	Product Information
TGA	Therapeutic Goods Administration
VDUAC	Victorian Drug Usage Advisory Committee
WHO	World Health Organization

CHAPTER ONE

Introduction

Millions of prescriptions for medications are written every year by medical practitioners (doctors), providing treatments for consumers (patients). A proportion of these treatments, however, result in further illness or injury, and in extreme cases, death.

The Second National Report on Patient Safety: Improving Medication Safety by the Safety and Quality Council of Australia (Roughead & Semple, 2002) reported that in Australia, between 1999 and 2000, two to three percent of total Australian hospital admissions may have been associated with medications. This equates to about 140,000 of the total 5.9 million hospital admissions across Australia.

According to Kohn, Corrigan and Donaldson (1999), the number of Americans to die each year from medical error is somewhere between 44,000 to 98,000 reflecting 2.9% to 3.7% of hospitalisations. Even using the lower estimate, at the time of the report, more people died in America in a given year as a result of medical errors than from motor vehicle accidents (43,458), breast cancer (42,297) or AIDS (16,516). Every year, over 6,000 Americans die from workplace injuries. The subset of these errors that are related to medications alone, occurring either in or out of the hospital are estimated to account for over 7,000 deaths annually, and two out of every 100 hospital admissions experienced an error that was considered preventable (Kohn, Corrigan & Donaldson, 1999).

The Therapeutics Goods Administration (TGA) in Australia is responsible for the quality, safety and efficacy of prescription and over the counter medicines marketed in Australia. Every medication that is approved for general use in Australia is first trialled by between 3,000 and 10,000 consumers. As the group of people who trial the drugs are small, medical practitioners and consumers can report any additional problems they notice when using these new drugs to ADRAC (Adverse Drug Reaction Advisory Committee) at the TGA. These reports are analysed by members of ADRAC and are then stored in a central database. The database now contains

30 years of data. Warnings about these new medications, which are based on these data, are collated by ADRAC and communicated back to the medical practitioners via a publication called *The Australian Adverse Drug Reaction Bulletin*.

Considerable knowledge exists about the properties of therapeutic medications (drugs), and the reasons why they may or may not result in unwanted non-therapeutic symptoms (adverse drug reactions). Knowledge may exist that relates to consumers in the general population or in specific groups such as women who are pregnant, or people with liver disease. What is unknown or partially known is: how this knowledge is used within a clinical setting when making decisions about drugs; and when there is so much information available, why preventable adverse drug reactions continue to occur. These questions provide a focus for this work.

This chapter will define the research problem to be addressed within this work in section 1.1, followed by the aims of the thesis in section 1.2. The research questions that have been posed to address the research problem and a rationale for those questions in section 1.3 are followed by an introduction to some terminology used within the work (section 1.4).

1.1. Research problem

The proposal for the research within this thesis arose from a problem raised by the Therapeutics Goods Administration (TGA), the central body in Australia for collecting voluntary reports from health professionals about suspected ADRs.

In the early stages of the work within this thesis, a General Practice Computing Group (GPCG) funded project was conducted to investigate methods of disseminating the ADR information collected by ADRAC back to prescribers. It began with the aim of creating a database from *The Australian Adverse Drug Reaction Bulletin* which contain new adverse drug reaction information, and determining where within the GP workflow this information could be incorporated to assist in providing up to date information that related to the specific consumer within the consulting room, at the time of prescribing. The results of this preliminary work have been documented in the Final Report to Department of Health and Aged Care for Contract for Services GPCG #12: Adverse Drug Reactions Improved Decision Support (ADRIDS) (O'Brien, 2001). An overview

of the processes used by the TGA to collect spontaneous reports can be found in section 2.2.5.1 of this thesis.

Data collected to inform the GPCG funded project included a series of four GP forums, interviews with four medical software companies that develop GP desktop software, and a forum with GP experts in health informatics from around Australia.

In addition to the work conducted through the GPCG funded project, a hospital pharmacist and a consumer who experienced a severe ADR were interviewed. The results of these interviews were documented in a University of Ballarat internal research report (O'Brien & Yearwood, 2002). The combined work from the GPCG project and the interviews with the hospital pharmacist and consumer form what is referred to in the remainder of this thesis, as the preliminary background studies.

Below are the key points that were highlighted from each of the initial data gathering phases in the preliminary background studies (O'Brien & Yearwood, 2005).

GP Forums

The perception of the group was that:

- ADRs occur infrequently within a community setting;
- the number of medications on the market is increasing. As a result, updating their knowledge about potential ADRs is also increasingly difficult;
- a computer program that sits in the background of their prescribing software would be useful. Because their perception is that ADRs occur infrequently, they believe it is a high priority to prevent them when possible, but a low priority regarding the time spent on ADR prevention compared with the other demands within their workload.

TGA discussions

The members of the TGA ADR team reported that:

- their primary role is to discover previously undocumented ADRs, to document them and alert the public as to their existence;

- background information about how the TGA ADR team operates was recorded. Detailed information about this can be found in section 2.2.5.1;
- a key element in identifying an ADR is to differentially diagnose between an ADR, the presenting disease, or a newly presenting disease. Generally this can be done with only a limited level of certainty, particularly if the ADR is one that has not been previously documented. Often it is not possible to do this differential diagnosis at the time the ADR occurs, but new ADRs can be discovered if prescribers report suspected ADRs. If there are enough reports from within Australia or around the world to produce a signal, ADRAC can be more certain that there is a relationship between a drug or group of drugs and a symptom or set of symptoms.

Consumer

This single case study highlighted the following:

- medical data for this consumer was stored in many locations. The consumer was the only person who knew where the complete medical history was located, and she was too ill to alert medical staff. She had experienced similar symptoms 10 years earlier, but had only limited information about that suspected reaction;
- the consumer made decisions that may have impacted on the outcome of the ADR. These decisions included: when to seek medical assistance, who to seek medical assistance from; and what information from her past medical history was relevant to relay to the doctor;
- having experienced a life-threatening ADR, she is highly motivated to prevent future ADRs.

Pharmacist

The pharmacist provided insight into the ADR reporting practices within a single Melbourne hospital. He also highlighted the following:

- if a person has experienced an ADR, ensuring the person has enough knowledge to prevent a second exposure to that medication was a high priority;
- accurate diagnosis is essential, although often extremely difficult. He stated that blaming a drug for an ADR means the person does not have access to that form of drug therapy

in the future. Not detecting the drug, results in an increased risk of the person being re-exposed to the same drug a second time.

Whilst conducting the preliminary background studies, a number of factors converged, which resulted in a fresh look at this problem, and a new understanding of this problem domain.

- Three key aspects to the ADR decision domain emerged from the preliminary work; prevention of ADRs, early detection and diagnosis of ADRs, and management of ADRs. Discriminating between the three stages was important.

- The results of the preliminary background work raised the question of the impact a system such as ADRIDS would have on prescriber decision-making. If a prescriber knows that a consumer may experience a particular reaction to a specific drug, would it alter their decision of what to prescribe? For example, if a consumer had a one in 10,000 chance of developing an ADR from one medication compared with a one in 50,000 chance for a different medication, would it alter the decision of which medication to prescribe? This information may be more likely to assist in detecting an ADR if it was suspected, rather than assisting in the decision of which drug to prescribe.

- There was an apparent disparity between the concern within the literature of the high incidence of ADRs, and the opinion of the GPs who participated in the forums that ADRs were sparse within a clinical setting, and so although ADRs are important to avoid and detect, they involved a small proportion of a GP workload.

- The hospital pharmacist was interviewed about the ADR data collection and reporting processes used within a large metropolitan hospital. It became clear that different groups within the ADR decision environment had different priorities about which aspect of the ADR decision domain was most important in the prevention, detection and management of ADRs.

- A consumer who had just experienced a severe life threatening ADR offered to record her story, in the form of a case study, for inclusion in the preliminary work. This case study highlighted a number of issues that indicated some limitations of current knowledge in the ADR decision domain.

The culmination of these events resulted in a new understanding of the problem. The key issues highlighted were that the ADR decision domain is more complex than a single decision-maker making prescribing decisions, and that there is a limited understanding of the ADR decision domain. In order to develop any decision support solution, a clearer understanding of the domain is required, otherwise systems will continue to be developed based on this limited knowledge of the domain, resulting in systems that provide only a partial solution.

1.2. Aims of the thesis

The overall aims of this thesis, arising from the problem described in the previous section, are to develop an understanding of: the ADR decision domain which will add to current knowledge of how ADR decisions are made; the problems that arise when making these decisions; and the complexities and the impact ADRs have on people.

The work of this thesis has three key purposes:

- to add to knowledge of this domain, so that it can be used by the decision-makers within this domain to assist in the prevention, detection and management of ADRs;
- to provide an understanding of the domain that can be used to inform the requirements analysis phase of ADR decision support;
- to determine the extent that the methodology used within this work can be applied to the requirements analysis phase in the field of software and/or systems engineering.

1.3. Research questions

The following research questions will be addressed within this work. Each question or group of questions will be followed by a rationale.

- Who are the decision-makers in the ADR domain?
- What decisions are made by each decision-maker?

The literature that has been reviewed in chapter two suggests that the majority of ADR decision support has been developed for medical practitioners, indicating that they are the primary decision-makers within this field. The preliminary background work (O'Brien & Yearwood, 2002) suggests that consumers are also involved in the ADR decision domain, and the decision types are broader than prescribing decisions. This work suggest that it is essential when attempting to design decision support systems, to know whose decisions are being supported, and which decisions need to be supported.

- What do decision-makers understand by the term ADR?
- Do all decision-makers agree on a definition of an ADR?

Once it has been established who within this domain are the people making ADR decisions, it is important to determine if all decision-makers have a similar understanding of the core concepts within the domain. To address these research questions, a symbolic interactionist philosophical perspective (discussed in detail in section 3.3) has been used. From this perspective, it is assumed that people from different groups will use the same terminology differently. In order to develop decision support that will be used by people from multiple groups, it is important to understand how they use the core terminology, and whether they use it in similar ways.

- How are ADR decisions made?
- What problems occur when making ADR decisions?
- What resources are used by decision-makers: information and knowledge sources and content?

To determine which decisions need to be supported, knowledge of how decision-makers currently make ADR decisions, which resources they use and the effectiveness of those resources, and where problems arise, will highlight where within the decision domain, support and new understanding is required. Understanding when and how ADR's occur, will provide an

opportunity to find solutions to the specific problem areas within the domain. There is likely to be a range of possible solutions to various aspects of the problem domain and these solutions may or may not involve decision support.

- How do ADRs affect people and how does this impact on decision-making?

ADRs can result in injury and illness from a treatment which is expected to assist consumers. Understanding the impact ADRs have on consumers, and understanding how this affects future decisions, assists in gathering a holistic understanding of this problem. It recognises that technology developed within this area is to assist humans, and an understanding of their experiences, may assist in developing solutions that take this context into account.

- How do decision-makers contribute to the creation of new knowledge at an individual, national and international level?

ADR knowledge is gathered by ADRAC from prescribers and consumers. It is analysed by ADRAC, and then fed back to prescribers. For completeness, this question has been included to understand the full cycle of ADR knowledge development and dissemination, rather than just understanding how the information is fed back to prescribers.

- To what extent can a grounded theory analysis of ADR case studies which include multiple views of a single instance of an ADR, assist in understanding the ADR decision domain to inform decision-makers and software and/or systems designers working within this area?

A method adapted from Information Systems (IS) research (discussed in detail in section 3.4.1) has been used to develop an understanding of a decision domain prior to developing decision support. This method arose from an awareness that the traditional requirements analysis exercise conducted in the preliminary background studies did not fully inform the decision domain.

1.4. Terminology

Most terminology within this domain will be defined in chapter two. A number of terms, however, reflect some of the preliminary assumptions underlying this work. They have been described in the following sections.

Consumer versus patient; medical practitioner versus doctor

Throughout this work, the terms 'consumer' and 'medical practitioner' have been chosen rather than 'patient' and 'doctor'. A social constructionist epistemology and symbolic interactionist theoretical framework, discussed in chapter three, assumes that members of each group within society interact using symbols or language to share meaning. An underlying assumption, therefore, is that members of different sociological groups may use terminology based on shared understanding within their own group. It is important, therefore, to use terminology that reflects the shared understanding of the sociological groups within this decision domain.

The term 'doctor' can be defined by the Macquarie Dictionary as "a person licensed to practise medicine, or some branch of medicine; a physician or medical practitioner other than a surgeon" (Macquarie University, 2001). As can be seen by this definition, 'doctor' and 'medical practitioner' are synonyms and therefore can be used interchangeably.

The term 'patient' can be defined as "1. one who is under medical or surgical treatment. 2. a person or thing that undergoes action (opposed to *agent*)", and the term 'consumer' can be defined as "one who uses a commodity or service (opposed to *producer*)" (Macquarie University, 2001). According to the second part of the definition of 'patient', a patient is acted upon, rather than someone who uses a service, which is the definition of a 'consumer'. The terms 'doctor' and 'patient' have implications within our society, therefore, that the 'doctor' is the person who *acts upon* a patient, and the 'patient' is the recipient of that expertise, who *is acted upon*. The terms 'medical practitioner' and 'consumer', imply that 'medical practitioners' provide a service, and 'consumers' are the purchasers or recipients of that service. As will be discussed in depth in section 2.3.6, the term 'patient' therefore is in line with Emanuel and Emanuel's (1992) paternalistic model of medical decision-making, whereas the term 'consumer', is more in line

with Emanuel and Emanuel's (1992) informed and collaborative models of medical decision-making.

It is acknowledged that at times a 'consumer' is a 'patient' in a medical system. That is, at times a health professional acts upon a person in the health care system, as in the case of a procedure such as an x-ray. In the case of ADR decision-making, as will be seen throughout the work of this thesis, the person with the suspected ADR may seek advice from a service provider about the nature of their symptoms, an act that is in line with the term 'consumer' of a health service, rather than 'patient' of a health service. The terms 'consumer' and 'medical practitioner' have therefore been used within the body of this work, rather than 'doctor' and 'patient'. The term 'medical practitioner', has been used for general practitioner, specialist or hospital based medical practitioner; it is the person who is being consulted. When important to discriminate between the types of medical practitioners, the terms GP, specialist, or hospital medical practitioner have been used.

Expert

The participants from ADRAC have been designated as 'experts'. The reason for this is that they work only with the diagnosis of ADRs, and have specialist knowledge in this area. By using this term, it is acknowledged that the experts have implicitly been placed at a higher level of importance, over and above that of the medical practitioners and/or consumers. This may appear to be incongruent with a symbolic interactionist theoretical perspective, where the emphasis is on accepting multiple perspectives equally. In the ADR area, it is the members of ADRAC who decide which of the reported suspected ADRs are likely to be ADRs, and which are more likely to have an explanation other than an association between the suspected drug and the newly presenting symptoms. The term 'expert' has been used to reflect this role ADRAC plays in the ADR decision domain.

Drug versus medicine

The term 'drug' is used to mean: a therapeutic medication that is available either through prescription or over the counter at a supermarket or pharmacy; or a complementary medication, such as an herbal remedy. The terms 'drug' and 'medicine' have been used interchangeably, as there does not appear to be a significant distinction between these terms. The term 'drug' however, is the term used by the medical community within the literature, and so it is the term

that has been used in this context. The term 'medicine' or 'medication' is the term most commonly used when speaking with consumers, to avoid the confusion with the use of the term 'drug' in our society to mean illegal drug.

Other terms used within this work have either been defined initially in chapter two, or have been informed by the data and have been described in chapter six.

CHAPTER TWO

Adverse Drug Reactions and Decision Support

2.1. Introduction

This research is about understanding the medical practitioner/consumer decision-making environment specific to adverse drug reactions (ADRs). The context is to broaden understanding to assist in the prevention, early detection and management of ADRs, and to consider if decision support may assist with this problem. Literature surrounding ADRs, medical practitioner/consumer decision-making, and decision support technologies, will be reviewed in this chapter.

The review begins by providing an understanding of ADRs in section 2.2 including ADR definitions (section 2.2.1), the incidence of ADRs in Australia and around the world, section 2.2.2), the reasons ADRs are known to occur (section 2.2.3), the types of ADRs that have been classified (section 2.2.4), a discussion of the attempts that have been made to reduce ADRs (section 2.2.5), and some national initiatives that will provide the infrastructure required to support ADR decision support applications (section 2.2.6). This will be followed by a summary of some of the problems that still need to be addressed within this domain.

The second component of this chapter (section 2.3) aims to provide an understanding of the decision processes surrounding ADRs. This section begins with an evaluation of current ADR decision support (section 2.3.1). This is followed by a discussion of a number of components of a decision support system, including: the ADR decision-makers (section 2.3.2), ADR decision types (section 2.3.3), the ADR decision environment (section 2.3.4), decision theories and technologies that may be applicable to this domain (section 2.3.5), and decision models (section 2.3.6). The final section in this chapter, section 2.4, will discuss literature that has used grounded theory to analyse case studies to assist in the software and/or systems design process.

2.2. Adverse drug reactions

2.2.1. ADR DEFINITIONS

There is some confusion within the literature about the definitions of ADRs. Terms used include Adverse Events, Adverse Drug Events (ADE), ADRs, Medical Error and Medication Error. In particular, the terms ADE, and ADR seem to be used interchangeably at times (Bates, 2000; Bortnichak & Dai, 1999), yet based on the definitions below, there is a significant difference between these terms.

2.2.1.1. Definitions of drug related events.

The Therapeutics Goods Administration (TGA), use the World Health Organization (WHO) definition of an ADR (WHO, 2004, Definitions Section)[1].

> 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 physiological function.

Adverse drug reactions can be defined further. The Therapeutics Goods Administration (TGA) is particularly interested in collecting data about serious and unexpected reactions that have not been previously documented, or where the incidence suddenly increases. Serious and unexpected reactions are defined below.

Serious Reaction

Again, the TGA use the WHO (2004, Definitions Section) of a 'serious reaction', below:

> A reaction which results in death, requires inpatient hospitalisation or prolongation of existing hospitalisation results in persistent or significant disability or incapacity is life-threatening.

[1] This style of referencing is recommended by the American Psychological Association. (2001, August 1). APA style for electronic sources. Available from http://www.apastyle.org. This style is used when the electronic source has no page numbers.

The TGA extend this definition to include birth defects and malignancy (Purcell, 2001).

Unexpected Reaction

An 'unexpected reaction' is defined by WHO (2004, Definitions Section):

> An adverse reaction, the nature or severity of which is not consistent with domestic labelling or market authorization, or expected from characteristics of the drug.

The underlying implication of each of the above definitions is that the reaction is related to the pharmacological properties of the drug.

Woodstock (2000) from the Food and Drug Administration in America describes an Adverse Event (AE) as "an undesired outcome that occurs during healthcare"(p. 2). She describes ADRs as AEs where there is a relationship between the undesired outcome and a drug. The definition of an ADR used by Woodstock (2000) is broader than the WHO (2004) definition, as it includes human error, rather that reactions directly related to the pharmacology of the drug.

Woodstock (2000) describes some of the problems associated with drugs, highlighting that " No drug is 100 percent safe; no pharmacologically active medicine exists that does not have side effects" (p. 2). Some of these ADRs, she says, however, are preventable. These have been listed below.

Defective product

- Error in the manufacturing of the drug

Medication error

- Prescribing
  - Calculating dosage
  - Prescribing the correct drug
- Dispensing
  - Reading handwriting
  - Understanding verbal medication errors
  - Dispensing the proper medication

Medical error

- Misdiagnosis
- Improper choice of treatment
- Failure to avoid drug interactions
- Failure to detect if the drug treatment is not working
- Failure to detect if the drug is causing further injury
- Failure to avoid allergic reaction

Consumer error

- Failure to understand instructions
- Failure to follow instructions
- Drug taken by someone other than whom the drug was prescribed

An adverse drug event (ADE) can be broadly described as any adverse event that is drug related whether it is as a result of a consumer being given the wrong drug or dosage, or related to the properties of the drug. Adverse drug reactions (ADR) are a subset of ADEs. Woodstock's definition above, is more in line with a definition of ADE, rather than the World Health Organization (WHO) definition of an ADR.

To re-iterate the key differences in these terms, an Adverse Event (AE), therefore is any medical event that results in an adverse outcome, such as surgery on the wrong leg. An Adverse Drug Event (ADE) is any event related to a drug or medication that results in an adverse outcome. This may be as a result of human or process errors. An Adverse Drug Reaction (ADR) is a drug related event that is related to the pharmacological properties of the drug that results in an adverse outcome.

It is acknowledged that ADEs and ADRs are highly interrelated, in that all ADRs are also adverse events and adverse events that are drug related. At times a result of this work may relate to an ADE as well as an ADR, however, as the scope of this work is limited to ADRs, implications will only be discussed in the context of ADRs. The following section (section 2.2.2, Incidence of ADRs) discusses the literature relating to ADRs. Due to the confusion in terminology within the literature between ADRs and ADE, it is necessary to highlight the inconsistencies within the literature when discussing these terms in an attempt to understand the

incidence of ADRs. The remainder of the work of this thesis will focus on implications that relate only to ADRs.

2.2.2. INCIDENCE OF ADRS

ADRs can cause death and injury, secondary illness, increased hospital stays, and sometimes require aggressive treatment to treat the ADR. In order to know the extent of the problem and to be able to measure long-term effectiveness, it is important to have some understanding of the incidence of ADRs.

The Second National Report on Patient Safety: Improving Medication Safety by the Safety and Quality Council of Australia, by Roughead and Semple (2002), describes ADRs as a particular type of adverse drug event (ADE) which includes side effects associated with medications.

Roughead and Semple (2002) reported that in Australia, between 1999 and 2000, two to three percent of total Australian hospital admissions might have been associated with medications (refers to ADEs). This equates to about 140,000 of the total 5.9 million hospital admissions across Australia.

The landmark report *To Err is Human. Building a Safer Health System* edited by Kohn et al. (1999) provides incidence figures which have been quoted extensively as a rationale for continuing research and development within this field. They state that the number of Americans to die each year from medical error is somewhere between 44,000 – 98,000 reflecting 2.9% to 3.7% of hospitalisations. These figures refer to adverse events (AEs). A major teaching hospital in the USA estimated that two out of every 100 admissions experienced a preventable ADE. Here the definition is of drug events, but the figures reflect preventable events rather than a total figure. This indicates that the total number of ADEs is in excess of two percent. As discussed in the previous section (section 2.2.1), ADRs are a subset of ADEs. ADR figures were not reported within this report.

Pirmohamed, Breckenridge, Kitteringham and Park (1998) from the University of Liverpool, state that five percent of all hospital admissions are caused by ADRs, and ten to twenty percent

of all hospital inpatients experience ADRs. They also state that ADRs are responsible for the death of 0.1% of medical and 0.01% of surgical inpatients.

Lazarou, Pomeranz and Corey (1998) reported the incidence of serious ADRs to be 6.7% and fatal ADRs 0.32%. They estimated from their studies that in 1994 in excess of two million hospital consumers had serious ADRs and over 100,000 experienced fatal ADRs, making this between the fourth and sixth leading cause of death in the USA. Interestingly, these figures are higher than those reported in *To Err is Human: Building a Safer Health system* (Kohn et al. 1999), but use the WHO ADR definition.

Jha, Kuperman, Rittenberg, Teich and Bates (2001) have developed a computer-based monitoring system to alert staff when an ADE may be present. Their aim was to measure hospital admissions caused by ADEs and to measure the associated costs. They concluded that 1.4% of admissions were caused by ADEs. They state in their introduction that drugs cause 20% of ADEs (That is, 20% of ADEs are ADRs). Using this approximate value, their study appears to indicate that 0.28% of hospital admissions are caused by ADRs.

Bates (2000) quoted Lazarou et al.'s article (1998) to emphasise the high incidence of ADRs, but then continued to discuss technology that may assist in the prevention of medication errors. Some of the suggestions include robots for filling prescriptions and bar coding of medications. In this case, Bates is referring to ADEs. This is a clear example of confused terminology. The incidence figures Lazarou used were in reference to ADRs, but the technologies suggested by Bates to assist with the problem relate to ADEs.

Estimating incidence is complicated by a number of factors. In addition to the difficulties surrounding ADR reporting, described in O'Brien and Yearwood (2002), there is the issue of medical staff recognising ADRs. This issue is important not only for estimating incidence, but also because early detection of an ADR and cessation of the medication can reduce the injury or illness caused by the ADR. According to Dormann, Criegee-Rieck, Neubert, Egger, Geise, Krebs, Schneider, Levy, Hahn and Brune (2003), four percent of all admissions to the hospital were due to ADRs, and in addition, another 4.5% were present. They also showed in their study

that over half of the ADRs were not recognised by either the admitting or the attending physician.

Between studies, there is a large variation in the estimated incidence of ADRs and ADEs. One study referred to ADRs and ADEs upon admission to hospital (Jha, Kuperman, Rittenberg, Teich & Bates, 2001), some to ADRs and ADEs that happen when an inpatient in a hospital (Kohn et al., 1999; Lazarou, Pomeranz & Corey, 1998), and some to hospital admission and whilst an inpatient in a hospital (Dormann, Criegee-Rieck, Neubert, Egger, Geise, Krebs, Schneider, Levy, Hahn & Brune, 2003; Pirmohamed, Breckenridge, Kitteringham & Park, 1998). Other reasons may include different definitions, data collection techniques or variations between hospitals and countries. It is clear from all of these studies that the incidence of Adverse Events, Adverse Drug Events and Adverse Drug Reactions result in a significant number of injuries and deaths, many of which are considered preventable, and that a significant proportion of ADRs are undetected, resulting in the injury or illness continuing beyond the initial incident.

As stated in the previous section, from this point forward the discussion will relate only to ADRs.

2.2.3. REASONS FOR ADRS

ADRs are known to occur for a number of reasons. They can be caused by drug properties, changes in their properties under certain conditions and drug interactions. Reactions can also be caused by the effects they can have on individuals. These individual consumers may have particular hypersensitivities, idiosyncratic absorption or metabolic characteristics, or particular conditions where particular drugs are contra-indicated.

The above reactions are triggered by the drugs themselves. Another set of reasons contributing to the incidences of ADRs may be related to the decisions made by those involved in the prevention, detection and management of ADRs in consumers.

2.2.4. TYPES OF ADRS

ADRs can be classified in multiple ways. Below, descriptions of Type A to F reactions, drug

interactions and contraindications are discussed. One source of information used in this section was an expert in ADRs from the TGA who provided information via personal communication (Purcell, 2003).

2.2.4.1. Type A

Type A ADRs are "predictable events or reactions, pharmacological reactions or expected events or reactions. They are common and are accounted for by a drug's known pharmacological properties" (Kalachnik, 1999). Purcell (2003) provided the example of respiratory depression due to a narcotic drug such as morphine which was used for treating severe pain.

2.2.4.2. Type B

Type B ADRs are unpredictable events or reactions: Also referred to as "idiosyncratic or unexpected events or reactions. These reactions are uncommon and independent of a drug's known pharmacological properties…They are considered the most serious and are potentially life threatening" (Kalachnik, 1999). This group includes hypersensitive reactions. A person may have a slight reaction the first time they are in contact with the drug, but may react more severely with each subsequent contact.

The key characteristics of Type A and Type B reactions have been summarised in Table 2-1.

Type A (augmented)	**Type B (bizarre)**
Pharmacological	Hypersensitivity or idiosyncratic
Dose related	Not dose related
Predictable	Unpredictable
Common	Rare
Usually not serious	Usually serious
Majority discovered before marketing	Majority discovered after marketing
Relatively low mortality	Relatively high mortality
Generally reversible (rapidly) with cessation of drug or decreased dose.	Generally not quickly reversible.

Table 2-1 Comparison between Type A and Type B ADRs (Purcell 2001)

2.2.4.3. Additional classifications of ADRs

Type A and Type B are the reaction types most commonly used by ADRAC. Edwards and Aronson (2000) expand these categories. These include:

- Type C, dose related and time related. Uncommon and related to the cumulative dose;
- Type D, delayed. Uncommon, usually dose related and usually becomes apparent some time after the use of the drug;
- Type E, withdrawal. Uncommon, occurs soon after the withdrawal of the drug;
- Type F, unexpected failure of therapy due to the intrinsic properties of the drug in question. Common, dose related and often caused by drug interactions.

Purcell (2003) expanded on Edward and Aronson's (2000) definition of a Type F ADR. A Type F ADR may signify a counterfeit medicine. A counterfeit medicine looks like a reputable brand name drug but has no active ingredient and is simply fraudulent. Other reasons for therapeutic failure include:

ADRs that result in therapeutic failure

- shortened shelf life due to breach of storage conditions, such as temperature and/or humidity;
- quality control problems during the manufacturing process, which may result in an inadequate amount of the active ingredient;
- the subset of 'vaccine failures' which are due to the properties of the drug, a small proportion of individuals who have been vaccinated will develop the disease notwithstanding the fact of prior vaccination.

2.2.4.4. Drug interactions

Drug interactions are ADRs that are caused by drug/drug or drug/food interactions (Kalachnik, 1999). According to Purcell (2003), reactions can also involve herbal remedies.

Purcell (2003) describes two subtypes of drug interactions, pharmacokinetic and pharmacodynamic.

Pharmacokinetic

Absorption, distribution, localisation in the tissues, biotransformation or excretion of one drug may result in an increased or decreased blood level or tissue level of the second drug/s.

Pharmacodynamic

Additive effects: An example is when two drugs are taken for hypertension, hypotension may be the reaction.

An additional complication is that the reaction to one drug may cause problems with a second drug. An example is a drug that causes vomiting may result in the second drug not being absorbed.

2.2.4.5. Contraindications (drug-disease interactions)

A final type of ADR can occur in consumers who have particular pre-existing conditions. If a drug is known to put stress on a particular part of the body, such as the effect of paracetamol on the liver, a consumer who has a condition which affects the liver such as cirrhosis, is likely to be more susceptible to the possible side effects of the drug, than a person with a healthy liver. Purcell (2003) explained that a specific drug is contraindicated by a particular condition. The contraindication is the condition/status which contraindicates the drug. Some drugs will be classified as absolute contraindications for consumers with a particular condition, indicating the drug **must never** be taken by a consumer with a particular condition, whilst other drugs will be classified as a relative contraindication for a particular condition, indicating the drug **should not** be taken by consumers with that specific condition.

2.2.4.6. The nocebo phenomenon

An additional complexity within the area of ADRs is the concept of the nocebo phenomenon, or the nocebo effect. This effect is similar to the placebo effect. When a consumer experiences a placebo effect, s/he takes a substance that has no effect, such as a sugar tablet, believes that the tablet will have a positive effect, and so experiences a positive effect.

The nocebo effect is when a consumer takes a substance that does not cause harm, again, such as a sugar tablet, but the consumer believes it may cause harm, s/he experiences harmful effects, which they perceive to be due to the drug. The complexities surrounding the nocebo effect will be discussed further in section 6.2.3.3.

2.2.4.7. Medical error

It is well documented that even though ADR types A to E are known to occur within the population, it is not possible at this stage to predict who will or will not experience a reaction, if the person has not previously been exposed to that particular drug and so they are not classified as 'error'. Preventable errors, such as prescribing a drug that is: contraindicated for a particular consumer; that a consumer has previously experienced an allergic reaction to; is known to cause a drug interaction; or caused by a manufacturing fault, can be classified, according to Woodstock's (2000) definition, as medical error. Failure to detect a Type A to E reaction is also classified, according to Woodstock's (2000) definition, as error.

Classifying error in this field however is difficult. It is clear which ADRs cannot be prevented, but defining exactly which ADRs are preventable is complex, and poorly defined. If two drugs are 'known' to interact in an adverse way, what is meant by 'known'? Generally the term appears to be used to mean well described and previously well documented in the literature. Is it assumed a medical practitioner will have access to all documented literature, or is it only considered an 'error' if it is documented in particular locations such as in product information? If a consumer has previously reacted to a particular drug, where is that information stored? It could be in one medical practitioner's file which is not accessible to a medical practitioner in another setting. The consumer may know about it, but only know it as labelled by a drug trade name, and not recognise the name of a newly prescribed drug.

Failure to detect a Type A to E ADR is also classified by Woodcroft (2002) as medical error. This definition, again, is problematic: failure to detect a suspected ADR within what time frame? At what point is it clear that an ADR has not been detected that 'should' have been detected? It is clear that this definition provides guidance about problems within the prescribing domain, but does not explicitly state at what point an 'error' has been made.

Several articles (Bates, 1999; Dean, Schachter, Vincent & Barber, 2002) including a report of the Victorian Drug Usage Advisory Committee on Drug Error Prevention in Victorian Hospitals (Australia) (VDUAC, 2002) called *Beyond blame*, emphasised that often error is caused by a combination or sequence of events, and that fostering a 'no-blame' culture with the aim of understanding why errors occur and managing them at a systems level that is co-ordinated is more effective than an approach at individual level of 'blame'.

2.2.5. EFFORTS TO REDUCE THE INCIDENCE OF ADRS

Understanding why ADRs occur, and exploring methods to increase this understanding are the first step in finding ways to decrease the incidence and severity of injury caused by ADRs.

Decreasing the severity of an ADR can be achieved by preventing the ADR or in cases where it was not possible to prevent the ADR, to detect it quickly to minimize the impact on the consumer.

Efforts to decrease the impact of ADRs appear to fall into six major categories: drug surveillance at a national and international level; clinical guidelines; desktop prescribing packages with built in alerts; hospital based alert systems; and education of both prescribers and consumers.

2.2.5.1. Drug surveillance - Australia

Drug surveillance assists in the prevention and early detection of ADRs by collecting suspected ADRs, documenting previously unknown information about the behaviour of particular drugs, and disseminating that information to prescribers. This can assist prescribers make decisions about who is most at risk of experiencing an ADR from a particular drug, and assist in identifying ADRs in situations where prevention was not possible.

ADRAC reporting processes

The ADRAC reporting processes were documented in the GPCG funded work that formed part of the preliminary background studies (O'Brien, 2001). These processes have been described below.

The TGA receives approx 13000 reports per year, of which approximately 7000 come in blue cards or a similar format. The blue cards include a defined number of fields and often contain additional information. The remainder of the reports arrive via phone, fax and occasionally by email. Reporting is voluntary, and is from medical practitioners, pharmacists and drug companies. GPs as a group report infrequently compared with the other groups.

Processing ADR Reports

On arrival, the reports are date stamped, triaged by a professional officer (nurse with Bachelor of Applied Science in Psychology). Reports of more serious reactions are channelled to the secretariat within the TGA. The reports are then annotated, highlighting the suspected drug(s), other drug(s), reaction term(s), relevant laboratory data, additional information, and then a causality rating is applied according to the committee's guidelines. If the reaction/interaction is 'unlabelled' this is drawn to the committee's attention, a check of the database is made to see if there are any other similar reports and MEDLARS is searched to ascertain whether the reaction has been published. Often workload is so great that this level of checking is not possible.

The reports are then transferred to clerical staff who number them, enter the data into the TGA database and check the data against the original report for accuracy. Overnight, a validation module updates the database by including the validated reports. For most reports (drugs of current interest and all reports mentioning WHO's critical reaction terms) a photocopy is made and forwarded to ADRAC for review at the next available meeting. The reports are then filed under the drug name(s). ADRAC meets eight times per year, reviews the more serious reports, discusses what action(s) it wants (more information, company comment, WHO data, literature search, ADRAC Bulletin item and other publication). Any corrections to the coding are made after the meeting and a subset of the data is then transmitted electronically to the WHO Uppsala Monitoring Centre.

Compiling an ADRAC Bulletin item

ADRAC identifies a drug safety issue from the reports reviewed. The secretariat then prepares an overview and/or a draft item for the *ADRAC Bulletin*. This involves looking at a summary printout for the drug, identifying the reaction(s) of interest, printing out the individual case summaries and aggregating the findings. This involves a 'pencil and paper' exercise to identify

such things as age and sex information, onset latencies (date arithmetic), doses, outcomes, laboratory data, and recovery times. The draft compiled by the secretariat is then considered by ADRAC at its meeting(s) (sometimes over six months). The draft is then edited and updated until accepted by the committee and ready for printing. 55,000 copies of the ADRAC Bulletin are distributed to Australian health professionals as well as overseas agencies.

Use of the TGA ADR database

TGA receives 2400 calls requesting information from the TGA ADR database per year. Of the calls, approx 60% are faxed. The remainder are phone and possibly once a week via the Internet. Occasionally there will be a request attached to the blue card that has been posted in.

Requests from the TGA ADR database

The usual question/requests asked are:

- What is the profile of a particular drug?
- What drugs are known to cause a particular reaction?
- Has a particular drug been known to cause a particular reaction?
- Sometimes they will ask for information about a particular case.
- When reporting a reaction – has this reaction been reported before?

Requests can come from pharmacists, GPs, pharmacists on behalf of GPs, hospital drug information services. The current database can produce three main reports.

Drug Summary - Type 9 report.

The report includes the following information;

- Single (generic) drug – multiple trade names;
- Reaction (preferred) terms listed alphabetically;
- Optional listing within system organ class.

This report is a simple line listing. It includes the number of reports that identify a specified reaction with a specific drug and can be generated at the time of a phone query by a doctor.

Reaction Summary – Type 19

- Lists all drugs against single (preferred) reaction.

Individual case report summary - Type 16 report

- Formatted anonymous details of individual reports.

Drug Surveillance programs both for pre and post marketing exist in many countries (ADRAC, 2001; Coulter, 2000; Grant, Coulson & Wood, 2000; Hartmann, Koller Doser & Kuhn, 1999; Jarernsiripornkul, Krska, Capps, Richards & Lee, 2002; Myhr, 1998; NAPRA, 2003; Orsini & Funk, 1995; Sutcliff, McMorran & Morawiecka, 2000). Once ADRs have been reported, collected and analysed, the information is then disseminated back to health professionals.

The pre marketing information is contained in approved product information (PI) available to medical practitioners and through products such as MIMS. Post marketing information is fed back to health professionals via *The Australian Adverse Drug Reaction Bulletin*, and to consumers via the *Consumer Medicine Information* (CMI).

In Australia, ADR reporting is primarily from hospital, pharmacist and general practice environments. Recently a consumer reporting system has also commenced. There is a telephone reporting system for consumers, the AME (Adverse Medicine Events) Line, that can be accessed by the National Prescribing Service web site (NPS, 2004). The line is manned by pharmacists who take the calls and make a diagnosis. The ADRs that are detected and meet the ADRAC reporting criteria are passed to ADRAC for processing.

Consumers Report on Medicines, Policy and Practice, (CRM, 2000) a policy that was adopted at the First International Conference on CRM in Sweden, talks about the limitations of ADR reporting systems that only include pharmacist and medical practitioners reporting. The document states that:

> …only a small proportion of practising physicians (often less than 5%) and a relatively small number of pharmacists (varying from country to country) contribute data to these systems: consequently information on suspected adverse effects communicated by a patient to his

> physician stands a 95% chance of going no further and making no contribution to the adverse drug reaction reporting system (section 1.2 para. 1).

This reinforces the need for consumer reporting such as the AME (Adverse Medicine Events) Line, mentioned above.

2.2.5.2. Drug surveillance - World Health Organization (WHO)

The World Health Organization (WHO) collects data from 72 countries around the world in an attempt to detect ADR signals that are too weak for any individual country to detect. (Lindquist, Edwards, Bate, Fucik, Nunes & Stahl, 1999; WHO, 2003). Some of the services WHO (2004) provides to the national centres includes: identifying new signals from the information submitted by the national centres; provision of the WHO database; information exchange between national centres and WHO; publications of newsletters and reports; provision of training and support to the national centres; and annual meetings of the representatives of national centres.

2.2.5.3. Clinical information and guidelines

The use of information and guidelines to assist medical practitioners with clinical decision-making is not a new concept. Guidelines for detecting and reporting ADRs exist in many countries around the world, and are often included with guidelines on reporting ADRs to the national reporting body (American Society of Consultant Pharmacists, 1998; American Society of Health-System Pharmacists, 1995; Naranjo, Shear & Lanctot, 1992; VDUAC, 1999; WHO, 2002). These paper based guidelines provide advice to medical practitioners and pharmacists about processes that can be followed that will assist in determining if the symptoms observed are likely to be associated with an ADR, rather than other reasons such as the existence of an ADE. An example is "Ensure that the medicine ordered is the medicine received and actually taken by the patient at the dose advised; Verify the onset of the suspected ADR was after the drug was taken, not before and discuss carefully the observation by the patient" (WHO, 2002, p. 14). If the medicine received was incorrect, or the dosage taken by the consumer was at an incorrect dose, the diagnosis is likely to be an ADE rather than an ADR.

One set of guidelines, described by the authors as an algorithm for ADR detection and diagnosis provided in-depth stepwise procedures to assist in the diagnosis of ADRs. This system uses statistical procedures, a Bayesian adverse drug reaction diagnostic instrument for determining the likelihood that the symptoms are an ADR (Naranjo et al., 1992).

The innovation, however, is taking the paper based information and guidelines, building them into clinical software, and developing search engines that assist in locating the information that relates to the specific consumer in the consulting room, at the time of decision-making (Barnett, Famiglietti, Kim, Hoffer & Feldman, 1998; Beliakov & Warren, 2001; Thomas, Dayton & Peter, 1999). Clinical information and guidelines have been shown to be most effective when integrated into the General Practitioner's (GP) decision-making process, and are linked to the actual consumer data (Beliakov & Warren, 2001).

PRODIGY (Prescribing RatiOnally with Decision-support In General practice studY) (SCHIN, 1998), developed at the University of Newcastle in the United Kingdom is one example of a clinical guidelines system that has decision support to assist in locating information at the time it is required by the consumer and the GP. The functionality within the system is described below:

> Following diagnosis, the GP is presented with clinical advice and therapeutic recommendations; information about non-drug treatments and consumer information leaflets is also included. The Phase Two system includes an extended choice of drugs, more comprehensive advisory texts and additional features such as Doctor-patient shared advice screens (p. 1).

One of the goals of PRODIGY phase two was to ensure the guidelines were based on best practice medicine, and that the drugs recommended were based on appropriateness, safety, effectiveness and cost. These guidelines also include advice about potential ADRs.

Therapeutic Guidelines, in Australia, is another organisation working towards incorporating their clinical guidelines, previously in textbook format, into GP desktop software with Decision support to allow the guidelines to be context dependent (*Therapeutic Guidelines*, 2004).

Information that was previously in text books or journals incorporated into software with decision support modules that locate the critical information the health professional requires at the time of decision-making is a significant step forward in assisting with medical decision-making. These systems are in the early stages of development and need to be highly tuned in order to assist in a medical environment. The GPs in ADR discussion forums indicated that if the information is too specific, too broad, too many alerts, takes too much time, is not relevant to the consumer within the consultation, the system is less likely to be used (O'Brien, 2001).

2.2.5.4. Electronic prescribing with ADR decision support modules

Electronic prescribing packages are becoming more popular in general practice clinics and are beginning to be introduced into hospital environments. Four packages were reviewed in the preliminary work for this project (O'Brien, 2001).

A GP may use the full features of the software, which often include a full electronic medical record, or they may only use the software for prescribing. Of the group of GPs who participated in ADR forums in the preliminary background studies, the majority used their desktop software purely for prescribing (O'Brien, 2001).

Decision support features built into these software products include access to product information, drug/drug interactions, drugs that are contraindicated for a specific condition and allergy alerts. The drug/drug interactions use a data source such as the MIMS Interact Database, or the A-Z Dex database (O'Brien, 2001).

Some of the clinical guidelines decision support systems (DSS) described in the previous section are designed to be embedded into clinical prescribing software or electronic medical records. GPs who participated in discussion forums in the preliminary work (O'Brien, 2001) discussed difficulties in using these products. Some of the problems they found were:

- Alerts are too frequent.
- Alerts are not graded according to severity.

- ADRs in product information (PI) sheets are conservative making it difficult to know during consultation how likely it is that an ADR will affect a consumer.
- PI that is available within these products discuss ADRs that are primarily from pre and post drug trials – spontaneous reporting data are in some of the PIs, but the process of including it can take up to a year.

One complexity raised in discussions with a member of ADRAC is that in many cases the frequency of a particular ADR is unknown and the information is therefore not available to be included within these prescribing packages. Another problem raised in the GP forums (O'Brien, 2001) is that the GPs often do not put the key information into these software packages, and so the alerts do not have the information they require to become activated.

2.2.5.5. Early warning ADR alert systems

The electronic prescribing packages mentioned above work with information about the drugs a consumer is taking or may take in the future, and limited medical history about the consumer such as known allergies, or significant medical conditions.

Hospital based alert systems which have a knowledge based engine use a body of medical history based on information collected whilst the consumer is a hospital inpatient. These systems warn staff if a consumer is showing early signs of reacting to a drug, or is at higher than expected risk of a reaction.

Raschke, Gollihare, Wunderlich, Guidry, Leibowitz, Peirce, Lemelson, Heisler and Susong (1998) developed a computer alert system with the aims of correcting prescription errors that may lead to ADEs and detecting ADEs before harm occurs. In this paper, the term ADE is used, but it fits within the definition of ADR used within the present study. The system they developed targeted a set of 37 known reactions. For each of the reactions, a set of vital signs have upper and lower limits. If a combination of these signs is registered an alert is triggered. Primary preventative alerts are triggered when a consumer may be about to have a reaction, and secondary prevention alerts are triggered when a consumer is experiencing a mild ADR. The

aim is to prevent ADRs progressing to serious ADRs. Of the alerts triggered, 54% were true alerts. The alerts identified opportunities to prevent injury at a rate of 64 per 1,000 admissions.

Another group of researchers has developed a clinical event monitor which scans electronic messages that contain new clinical and administrative information sent between clinical computing systems, or within an individual system, and notifies medical staff of any patterns that indicate there may be a problem that requires attention (Payne, Savarina, Marshall & Hoey, 2000). The system triggers during order processing, admit, discharge and transfer movements. The system monitors events such as alerting the ADE coordinator if drugs are ordered that may indicate an ADR has occurred, dose checks and drug interactions. Again, the system works on business rules. The system described by Payne et al. (2000) is limited to eight rules. Their conclusion is that although the system has proven useful, development of the business rules is an iterative process that is complex.

Alert is a clinical decision support tool developed by the Baptist Health System (Caldwell, 2000). When a consumer is admitted to hospital, admission and demographic information is fed into their clinical data repository. Whilst the consumer is in the hospital, information is collected including laboratory results, medications, diet and radiology. As in the previous two systems, the data are passed through a rule-based module and alerts are triggered if certain criteria are met.

These systems are hospital based and require medical records to be electronic. They are rule-based, which like any medical rule-based system, requires frequent updates due to the rate of change in medical knowledge. Most of these systems have also been used to estimate the number of ADRs occurring in a particular hospital setting (Bates, 2000; Caldwell, 2000; Payne et al., 2000; Raschke, Gollihare, Wunderlich, Guidry, Leibowitz, Peirce, Lemelson, Heisler & Susong, 1998). These systems are currently in the research stage, and are not fully implemented.

2.2.5.6. Awareness, information and education

Prevention is primarily about minimizing a consumer's risk of taking a medication that may cause injury. Prevention also includes the detection of ADRs as soon as possible in order to prevent ongoing injury.

Many articles distinguish between preventable and unpreventable ADRs and make suggestions about prevention (Bannwarth, Queneau, Carpentier, Guliana, Bouget & Trombert, 2003; Brown & Landry, 2001; Cohen, 2000; Dormann et al., 2003; Geyer, 2003; Lachs & Boyer, 2003). Strategies include taking a detailed case history of reactions to drugs, awareness of consumers who are at high risk (such as the elderly on multiple drugs), the use of databases (electronic and manual) to check for interactions, to be aware of which drugs are more likely to cause interactions and family history of reactions to medications which may require a tailored approach to medication management for consumers (FDA, 2002).

Lachs and Boyer (2003) have produced an article for the consumer titled *Seven steps to safer drug use*. This article describes the things that a consumer needs to advise his/her health practitioner about even if the medical practitioner does not specifically ask. They discuss the disclosure of all medications, prescription, non-prescription and complementary. They discuss disclosing this information even if the medical practitioner is not prescribing a new medication, as the current symptoms may be related to a medication they are taking. They also discuss mentioning all allergies they have had in the past, as a drug that is being prescribed may be of the same drug class or 'family' of drugs, and so should be avoided.

Information to assist with ADR decision-making has been another focus of prevention and early detection. The focus has been on providing up to date newly described ADRs relating to: old medications, or medications that are new on the market, product information, drug interaction information, drug-disease interaction information primarily to prescribers and consumer information sheets for consumers.

2.2.6. THE AUSTRALIAN CONTEXT

Australia has a number of state and national projects under development that will add infrastructure that will assist with this problem.

2.2.6.1. Health Online

The *Health Online* is a national plan for health information management for Australia. The key objectives include: achieving national collaboration; laying sound foundations in the areas of privacy laws; security and standards; empowering consumers; supporting clinical care; using

information to build a more efficient and effective health care system; and to exporting telehealth and health informatics services.

Health Online has identified a number of national projects, including electronic decision support, electronic health records, *HealthInsite*, *MediConnect*, standards and privacy (*Health Online*, 2004). Key projects that relate to drug safety have been discussed in the following sections.

2.2.6.2. Electronic Decision Support

In 2002, the National Institute of Clinical Studies (NICS) and the National Health Information Management Advisory Council (NHIMAC) jointly sponsored the Electronic Decision Support Governance Workshop, (Phillips, 2002) which aimed to identify the key issues and priorities for governance in the area of clinical decision support, and then to bridge the gap between research and clinical practice. This report relates to Electronic Decision Support Systems (EDSS) in health. It is not specific to decision support related to ADRs.

Within the report, the authors stated that although decision support is an important new development to assist clinicians who are overloaded with new information, the development has been fragmented and uncoordinated leading to problems of accessibility, scalability, duplication and lack of integration with existing systems. This initial workshop resulted in the establishment of a National Electronic Decision Support Taskforce to address the key priorities that were identified within this initial workshop.

Phillips (2002, p. 5) listed the issues to be addressed by the taskforce. They included:

- the current activity and expenditure in the electronic decision support sector;
- evidence of effectiveness of the different EDSS in improving outcomes;
- consultations with stakeholders in relation to their business needs (e.g. software industry and their information needs (e.g. clinicians and other end users);
- areas of highest priority for national governance in terms of health outcomes, improved delivery of research evidence into practice and improved quality and safety of decision support systems.

The report included within the appendices the responses from 27 organisations to a pre-workshop survey as well as presentations from five keynote speakers. The following key issues were highlighted by participants within the workshop (Phillips, 2002). Several of these issues have been addressed by the research in this thesis:

- The NSW Health Department stated one of their priories as "Modelling the clinical decision-making process to identify the business processes that require decision support and determine what form of decision support is appropriate" (p. 44).
- The Health Advisory Committee/NHMRC and University of Queensland included as a priority "developing interfaces designed for how people really work – that is not just 'user friendly' but designed to be intuitive and less rather than more work than non-EDS system" (p. 49)
- The Consumer Health Forum said "ongoing consultation with consumers around ehealth initiatives in a more general sense including decision support, integrated health records etc." (p. 64).
- "The flexibility and facility for consumer empowerment and self-management as well as allowance for input from consumers during the health encounter. The issue of 'compliance'[2] needs to be reframed in terms of empowerment" (p. 64)

2.2.6.3. Health Connect

Health Connect (2004) is an electronic medical record that has been proposed and is being developed for use in Australia. It is currently in its second phase of development. The *Health Connect* concept is that health information would be collected by the health service provider at the point of care and stored in a standard format. Health providers, with consumer consent, would be able to access previous episodes of care from health providers, regardless of its location. Consumers would also have access to their records. The information would contain summaries of the episode of care, not all of the details.

[2] Recently the term 'concordance' has begun being used by some medical practitioners in an attempt to recognise shared decision making.

Advantages of this concept include: allowing consumers to have more control over their information; allowing consumers to participate actively in decisions about their health; improving the speed of access and accuracy of information enabling more time for direct services to the consumer; reduction in the duplication of services; improved portability of health records and exchange of information between providers; and better information for research and the development of policy and planning (*Health Connect*, 2004).

Phase one of the project has been completed. Phase two will occur between 2003 and 2005. The key objectives are to demonstrate value and feasibility, develop a robust business case for proceeding, finalise the design, select system components, commence the process for integration with systems such as *MediConnect*, continue developing other essential building blocks for an electronic health record, ensure stakeholders are informed and ready, and develop a national implementation plan.

This is another example of a positive step forward towards integration of medical information. An electronic health record that allows access to previous medical records will assist with ensuring a full case history is available. The issue remains that putting all of the information together, is a first step. Knowing what is in a large record, however, and being able to access key factors is another issue. If, within a ten year record of event summaries, there is a record highlighting a suspected ADR, the question is whether either the consumer and/or prescriber will know it is there, and think to read it. Having information in textual event summaries, will be like having yet another source of data available, such as guidelines or *The Australian Adverse Drug Reaction Bulletin*, for both the consumer and prescriber to access. The next phase will be to develop decision support software that can assist in retrieving critical elements from the episode of care summaries, and bringing them to the attention of the decision-maker at the time of decision-making.

2.2.6.4. HealthInsite

Hopkins and Fogg (2002) discussed the issue of accessing health information via the Internet. They stated that consumers have concerns over the quality of the information on the Internet, however value the convenience and access to such a wide variety of resources that can be accessed to provide in-depth health advice.

HealthInsite was first piloted in 1999 by the Commonwealth Department of Health and Ageing to provide Australians with high quality, relevant information. According to Hopkins and Fogg (2002), the feedback about the site was generally positive, and the concept was well received. Issues such as promotion of the site, ensuring all levels of users can access it easily, and in particular ongoing review with consumers as the site develops.

An aspect of the *HealthInsite* project that pertains to ADRs, is that it contains information about conditions and diseases, and treatment options. There are plans to include *Consumer Medicine Information* leaflets in the future.

2.2.6.5. MediConnect

MediConnect (2004) is a project that has the aim of creating summaries of medication records which will be available to service providers, with consumer permission, regardless of which service provider created the record. *MediConnect* aims to reduce the incidence of adverse drug events by improving consumer and health care access to complete medical information.

The electronic medical record will be stored with the Health Insurance Commission (HIC). Service providers will be able to access these records when necessary. The only service providers to access the records, and new medications will only be added to the record with consumer consent.

The record will hold identifying information and also information about previous adverse drug reactions. The record will include not only prescription medications, but also over the counter and complementary medicines. Information about why the medication has been prescribed will also be included. This project is currently being trialled in Ballarat and Launceston.

A centralised medications record will assist with the reduction of adverse drug reactions in areas such as drug interactions and a recorded history of previous adverse drug reactions. This system will become significantly more useful in the prevention of adverse drug reactions if it is connected to drug interaction databases.

This initiative, again, is a significant step forward in the integration of health information. Again, in order for it to be useful to ADR decision-makers, the decision-makers need to think to access the information, and they need to consider the possibility that the symptoms the consumer is exhibiting may be related to one of the drugs they are taking.

2.2.6.6. Standards and Laws

There are some key issues that need to be resolved before any form of electronic health information exchange can occur. Unless consumer health information is secure and privacy can be ensured, consumers will not be prepared to endorse information sharing. As of January 2004, a proposed privacy code, which has been developed and available for public comment, is before health ministers for consideration (*Health Online*, 2004). A copy of the code is available at www.health.gov.au/pubs/nhpcode.htm.

Without national and preferably international data and technical standards, communication between systems is arduous, and information integrity may be compromised. The Information and Communications Technology Standards Committee (ICTSC) has developed a plan *Setting the Standards: A National Health Information Standards plan for Australia.* This can also be accessed on the *Health Online* web site (*Health Online*, 2004).

Standard drug names and drug codes, standard methods of transporting clinical and medical information between service providers, consumer rights that include privacy and security of their information are all building blocks required to allow electronic data to be shared. The concept of shared electronic data is a cornerstone for the development of electronic clinical decision support systems, as it will allow the key information to be accessible to the ADR decision-makers at the time of decision-making. In addition, in order for a decision support system that has been developed to be transportable to other sectors, a standard infrastructure is essential.

2.2.6.7. Clinician's Health Channel

The *Clinician's Health Channel* (2003) is a Victorian Government initiative with the aim of providing clinicians, which includes medical practitioners, nurses and allied health professions in the Victorian public health sector, quality information relevant to Australian clinicians.

The *Clinician's Health Channel*, provides prescribers with access to a wide variety of electronic databases including Drug Product Information, the Australian Medicine's Handbook, Mims, Micromedix which includes a drug interaction tool and alternative medicine information, Therapeutic Guidelines, and access to the National Prescribing Service. It also includes access to a number of bulletins including *The Australian Adverse Drug Reaction Bulletin*.

This is an example of a system, which provides access to a very wide variety of drug information and drug safety resources. The issue remains, however, that in order to access this information to prevent and detect ADRs, a prescriber needs to realise that there is information available that they need to access, and access the information at the time within their workflow that they need it.

2.2.6.8. Better Health Channel

The *Better Health Channel* (2003) is the equivalent of the *Clinician's Health Channel*, but for consumers. It provides a range of information about medicines, and the consumer Medication Information sheets are available via this site.

2.2.6.9. Consumer Medicine Information

The *Consumer Medicine Information* (CMI) is information aimed for consumers and is available for all prescription medications and some over-the-counter and complementary medications. This leaflet is the consumer equivalent of the product information sheets for medical practitioners. These leaflets will soon be available via the NPS web site, but are currently available on the *Better Health Channel* (2003).

In the last year (2003-2004), the National Prescribing Service in Australia (NPS) have continued to develop resources to assist consumers make decisions about medications. These include a consumer information line (*Medicines Line*), general information about medicines (*Medimate*), and a consumer newsletter produced by consumers for consumers (NPS, 2004).

The consumer drugs and information line provides a facility for consumers to ask pharmacists questions about medications including prescription, non-prescription and complementary, and to report suspected ADRs.

Medimate provides more general information about medicines and is available for consumers to print or view over the Internet. This product encourages consumers to work with their medical practitioner and pharmacist, but also assists consumers make their own decisions by providing up to date information using non-medical language.

This initiative is a positive step towards providing consumers with access to reliable information. Some positive aspects of these sheets are that as well as including specific information about the drug, they also include information about consumer behaviour, and information that the consumer must tell the medical practitioner and/or pharmacist. These areas are very comprehensive.

Problems with the information sheets are that each of the CMI is four pages in length in fairly small print so a consumer would need to be fairly motivated to read it all in detail, and have adequate eye sight. The sheets state that they do not contain all of the available information, which raises the questions of how a consumer does access all available information, and what other information there is to know about the medication that is not stated on the sheet. Although there are many medical terms defined, there remains medical terminology that would not be understood by the average person, such as in the information about Tramal. This sheet states that you must tell your medical practitioner if "you are known to be sensitive to opioids" (*Better Health Channel*, 2003, Tramal(R) SR Sustained Release Tablets). This implies that the consumer understands that opioids are a class of drugs, and knows which drugs belong to that class.

2.2.7. ISSUES WITH EFFORTS TO REDUCE ADRS

As can be seen from sections 2.2.5 and 2.2.6, there have been many developments within this area to either, directly reduce illness and injury caused by ADRs or indirectly through improved infrastructure. Many of these systems are still at the research or planning stage, and have yet to be implemented.

Having reviewed the literature associated with the efforts that have been made to reduce ADRs, a number of issues remain including the following:

- Drug surveillance systems work on voluntary reporting, and many ADRs go unreported.
- Drug alerts within GP desktop systems at this time alert too frequently and the drug information provided is too broad to be useful.
- The likelihood of a specific drug causing an ADR for a specific consumer is not known if the consumer has not previously taken the drug.
- Hospital alert systems use rules which need to be updated frequently. They are useful for consumers being monitored in hospitals but do not generalise to community settings.
- The majority of ADR decision support is for the prescriber, rather than providing support for multiple decision-makers.
- There are many information sources that are now available on the Internet. The information is in multiple locations using a variety of search options. There is duplication between *HealthInsite*, a commonwealth initiative and the *Clinician's Health Channel* and *Better Health Channel* which are state initiatives. These systems are only useful if the decision-makers realise that the symptoms may pertain to an ADR, and think to access them.

The preliminary background studies suggested that the current understanding of the ADR decision domain used to develop the systems described above is limited, and there are many additional sources of information that may be used by prescribers and consumers currently that are not included in these systems, (O'Brien & Yearwood, 2002). It is also not clear how the information is used within the prescriber workflow.

Within the work of this thesis, an aim is to learn more about these information sources, understand more about how people currently use the information that is available, who the key decision-makers are within the domain, the nature of the decisions being made and the additional requirements people have that may be able to assist in the prevention, early detection and management of ADRs.

Having explored adverse drug reactions in the current section, the next section provides an overview of decision-making, including a diagram illustrating the key components involved in

developing a decision support system, discussion about who the decision-makers are within the ADR environment, the ADR decision environment, key domain characteristics and some decision support techniques that may be useful in this domain.

2.3. Decision support

The work described in this thesis is exploratory in nature. As the context of this work is whether decision support may be able to assist with the prevention, detection and/or management of ADRs, a general overview of decision support systems and their potential application to this area has been included below.

The development of a decision support system may use a range of building blocks. These have been visually represented in Figure 2-1, below.

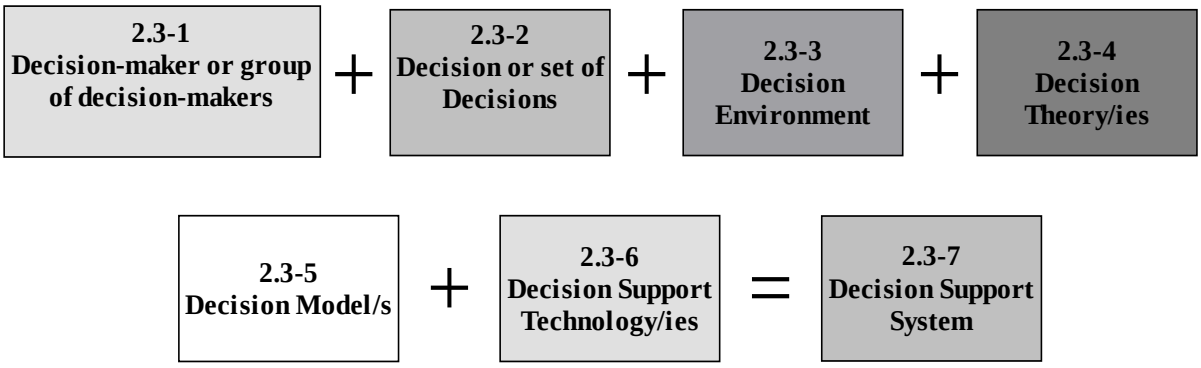

Figure 2-1 Building blocks for the development of a decision support system

Decision support systems have been developed for use across many different discipline areas, and as a consequence, different people have different understandings of decision support concepts. When discussing decision support with a general practitioner, an example of a decision support system raised may be the medical practitioner's desk top prescribing package that has a built in alert signalling when two drugs prescribed may result in an interaction. In contrast, a manager of a company may see decision support as a software package that will utilise years of operational data stored in a data warehouse to forecast future trends that may assist with decisions about marketing.

A psychologist may refer to a decision theory as a theory that has been developed to explain how a human makes decisions using a particular perspective such as from a behaviouralist's or a naturalistic perspective. A computer analyst from the field of decision support, may be more interested in prescriptive decision theory, such as Utility Theory, that can be applied to the development of a computer system that takes into consideration preferences, risk and uncertainty, and utilises probability to determine the 'best' decision based on the parameters input into the system. The psychologist's focus may be more on what do humans currently do. The computer analyst's focus may be more about how can software replicate and 'improve' decision-making processes.

To assist with clarity, an explanation of how these terms have been used within the decision support domain have been described below. The first two definitions, 'Decision', and 'Decide' are from the Merriam-Webster (2003) online dictionary. The remainder are definitions based on how the terms have been used within this work:

Decision: the act or process of deciding.

Decide:

- to arrive at a solution that ends uncertainty or dispute about (decide what to do) to select as a course of action—used with an infinitive (decided to go)
- to bring to a definitive end (one blow decided the fight)
- to induce to come to a choice (her pleas decided him to help)
- **intransitive senses**: to make a choice or judgement.

It is the final component of this definition that is applicable to the ADR decision domain. The medical practitioners in an ADR domain appear to be more likely to make a judgement based on the most likely possibility, rather than making a definitive choice that ends uncertainty.

Decision Support: Assist with the act of deciding. Based on the definition for decide, the goal of decision support is to assist in making a decision to a greater level of certainty than without the decision support, or to prompt that a decision needs to be made. Assistance may be in the form of technical or non-technical support. Methods may be as simple as a decision flowchart on a wall, through to a fully automated system that can make autonomous decisions.

Decision Theory: A number of theories of decision-making. This may include theories to describe how humans currently make decisions, theories that attempt to suggest methods of increasing the effectiveness of decision-making based on some criteria of 'effective', or theories that attempt to predict future decisions based on past decisions.

Decision Model: A generic model generally implies a representation of a larger scale real world object. The representation is generally simpler, smaller, and includes the key features. A decision model attempts to provide a similar function. It describes a series of steps or processes, in a simplified form of decision-making based on a specific decision theory or group of decision theories.

Decision Support Technology: Tools that have been used in any domain to develop a decision support system. These tools may be in the form of database concepts such as data warehousing, tools based on statistical analysis such as probability, Bayesian techniques, neural networks, markov models, or systems that use a range of tools such as rule-based systems, expert systems, case-based reasoning, agent technology.

Decision Support System: A specific group of systems that support decision-making. The support can be in the form of providing information at the time the decision-maker requires it such as computerised clinical guidelines, or make fully autonomous decisions such as the autopilot functionality found within aeroplanes. A decision support system may or may not use technology.

2.3.1. EVALUATION OF CURRENT ADR DECISION SUPPORT

The current strategies that are being used to assist in decreasing the incidence of injury caused by ADRs have been evaluated. These strategies were described in section 2.2.5. They included: drug surveillance in Australia; drug surveillance world wide; computerised clinical guidelines; electronic prescribing with ADR decision support modules; early warning ADR alert systems; and increased awareness and education. In this section they will be reviewed using Figure 2-1 as a framework for discussion. The results of this evaluation are in Table 2-2.

	Aim	Decision-maker/s	Decision type/s	Decision environ-ment	Assumptions and underlying decision theory	Decision model	Decision support technology
Drug surveillance	Develop new ADR knowledge. That is discover 'unknown' ADRs so they become 'known' Assist in the prevention and detection of 'known' ADRs	Health professionals via newsletters and updates to product information. Consumers via consumer medical information and media	Prescribing and diagnosing decisions.	Regulatory environment	Humans need information to make decisions. Provides information to decision-makers, but assumes the medical practitioners have strategies to make the decisions.	No underlying decision model.	Data mining to assist in signal detection. No decision support technology used to disseminate the information.
Clinical guidelines	To provide ADR information to prescribers in a useful format at the time of making decisions.	Medical practitioners and pharmacists	Prescribing, detecting and diagnosing decisions	In clinical environment	**Cognitive theory:** Medical practitioners and pharmacists cannot hold all of the essential information in their memory, do not have time to keep up to date with large quantities of drug information, and may not have the time to consult a manual.	**Decision model based on a prescriptive theory**: Rule-based decision support. Provides decision rules to decision-maker at the time of prescribing so s/he can use them if required.	Paper based guidelines use no technology. Context sensitive search engines.

	Aim	Decision-maker/s	Decision type/s	Decision environment	Assumptions and underlying decision theory	Decision model	Decision support technology
Electronic prescribing with ADR decision support modules	**Prevent 'medical error'.** Warn a prescriber if s/he is prescribing a drug that is known to cause harm to a consumer: ▪ Drug interactions ▪ Drug contraindication ▪ Consumer past allergies	Prescribers	Prescribing decisions	Clinical environment	**Cognitive theory:** Medical practitioners cannot hold all the essential information at one time, and may make an error. This system attempts to assist in the prevention of these known preventative errors.	No underlying decision model	Uses **simple rule-based technology** to interrupt work flow if drug prescribed is not allowed based on a rule in the rule engine
	Product information available within the software package to lookup if required.	Medical practitioners	Prescribing and diagnostic decisions[3]	Clinical environment	**Cognitive theory:** Medical practitioners cannot hold all of the essential information in their memory and may not have the time to consult a paper based manual.	No underlying decision model	Uses **search engines** to facilitate easy searching of electronic source, and can be updated regularly and easily.

[3] If a prescriber has a hypothesis that a drug may be associated with the consumer's symptoms, consulting the product information can assist in strengthening or weakening the hypothesis, thus assisting in diagnostic decision-making.

	Aim	Decision-maker/s	Decision type/s	Decision environ-ment	Assumptions and underlying decision theory	Decision model	Decision support technology
Early warning ADR alert systems	Detect a suspected ADR before it has time to do harm	Hospital staff, medical practitioners and nurses primarily	Detection of suspected ADRs	Hospital environment	Heuristics (rule of thumb) If a particular set of symptoms occur, suspect an ADR.	No explicit decision model defined	Uses **a rule-based engine**. If the consumer symptoms including lab test results and biometrics match a set of conditions, the rule-based engine triggers an alert.
Awareness, information and education	To provide information to medical practitioners, consumers and pharmacists about risks of medicines	Medical practitioners, consumers and pharmacists	Prescribing, diagnostic and information sharing	Non specific	No underlying decision theory.	Education model	Not technology based.

Table 2-2 Decision theories, models and technologies underpinning current ADR prevention and detection strategies

As can be seen from this evaluation, each system has a specific purpose, and is targeted towards a particular group of decision-makers, in the majority of cases, the medical practitioner. The decision theory underlying the systems is implicit, but in most cases has not been explicitly stated, although as can be seen, they all have some underlying theory. The technologies that have been used primarily include rule-based engines and advanced search engines.

The analysis of these strategies has also revealed some assumptions underlying the development of these systems. They assumed that:

- the primary decision-maker in the ADR decision domain is the medical practitioner. Technology in clinical and hospital environments, therefore, is designed for the medical practitioners on behalf of the consumers;
- that medical practitioners know how to make ADR decisions and have robust strategies. These systems, therefore, assist medical practitioners make decisions by providing up-to-date accurate information at the time of decision-making;
- that medical practitioners cannot hold all of the required information about drugs and drug safety in their memories, and will benefit from having the information easily available and key information provided to them at the time of decision-making;
- that medical practitioners are likely to use their own drug and ADR knowledge rather than access up-to-date information if they are time constrained, and so providing the up-to-date information at the time of decision-making will assist the medical practitioners to access this up-to-date information;
- that consumers require some ADR information, but different information to medical practitioners;
- information to consumer is best provided in written format.

The preliminary background studies (O'Brien & Yearwood, 2002) suggest that some of these assumptions may not take into account the complexity of the ADR decision domain. The focus of the work of this thesis is to explore the ADR domain in order to understand the complexities.

The following sections will, again, use the components of decision support described in Figure 2-1 , to provide an overview of current knowledge that could be used within this domain, and to highlighting the gaps within this area.

2.3.2. ADR DECISION-MAKER OR GROUP OF DECISION-MAKERS

To develop decision support, an obvious question is, whose decisions require support? The primary decision-maker to use decision support in the ADR decision domain, listed in Table 2-2, is the medical practitioner, including GPs, specialists and hospital medical staff.

There is a significant body of research addressing the role of consumer decision-making within a medical context, however the decision type is primarily limited to treatment decisions (Bankhead, 1999; Benson & Britten, 2002; Bruera, Willey, Palmer & Rosales, 2001; Charavell, Bremond, Moumjid-Ferdjaoui, Mignotte & Odile Carrere, 2001; Coulter, Entwistle & Gilbert, 1999; FDA, 2003; Mcvea, Minier & Johnson Palensky, 2001; Mussi, 1999; Scott & Lenert, 2000).

Another subset of decisions consumers are known to make within this domain, are decisions about when to report a suspected ADR. In some countries, consumers report suspected ADRs to health authorities (NAPRA, 2003; Safety and Quality Council, 2003; TGA, 2003) The introduction of the *Medicines Line*, in Australia (discussed in section 2.2.6.9) encourages consumers to report suspected ADRs.

The preliminary background studies (O'Brien & Yearwood, 2002) indicated that the ADR decision-makers may be broader than an individual medical practitioner, and may include multiple medical practitioners, the consumer and the pharmacist, and consumer decision types are broader than treatment and reporting decisions. An aim of this work is to understand more about the decision-makers within the ADR decision domain, and determine the types of decisions made by each of these decision-makers.

2.3.3. ADR DECISIONS OR SET OF DECISIONS

The decision types supported by the decision support strategies listed in Table 2-2, included prescribing, detecting and diagnosing decisions made by medical practitioners, and assisting consumers to know when to share information.

The drug surveillance systems aim to identify previously undocumented ADRs, or ADRs that have increased in frequency with the aim of providing information to prescribers at the time of prescribing. These systems assist with the decision of 'which drug to prescribe?' and 'is this set of symptoms associated with a particular drug?' by providing information to prescribers. The computerised clinical guidelines and the drug dictionaries embedded within GP desktop software assist, again, with making decisions about which drug to prescribe. They may also provide additional information such as contraindications for particular groups of consumers within the guidelines, or the specific consumer within the consultation room in the case of the desk top prescribing system. They add to the information available to make these decisions, however, they still address the same two questions. The hospital based systems which provide an alert if a suspected ADR is detected, also assist with the decision 'is this set of symptoms associated with a drug?' They also provide additional assistance by raising the question initially, without waiting for alternative diagnoses to be exhausted prior to considering this decision.

Appendix six of the ADRIDS preliminary work (O'Brien, 2001), lists a number of decision types within the ADR decision context. The following decisions were derived from the decision types elicited from the group of general practitioners in the forums from this work. These include:

Prevention

- deciding which drug to prescribe;
- deciding which information to provide when a consumer asks about a specific drug;
- deciding which information to provide when a consumer requests information about potential side effects of a drug prescribed for him/herself or a family member;

- deciding which information to provide when a consumer requests information about potential interactions between a newly prescribed drug and a drug s/he is currently taking;
- deciding which information to communicate to a pharmacist when dispensing a drug;
- deciding whether to trial a new drug on the market;

Early detection or management

- making a differential diagnosis of a disease versus an ADR, either face to face or via a telephone consultation when a consumer phones or presents about a possible reaction having commenced drug therapy;
- determining whether to cease a drug, which drug to cease, and when to cease it;
- deciding whether to report an ADR to the TGA;
- situations when the consumer is describing symptoms that may be caused by a reaction;
    - the GP formulating diagnosis of ADR as a possibility;
- situations when a drug company asks for information about reactions observed;
    - the drug company formulating diagnosis of ADR as a possibility.

As mentioned in the previous section, the primary decision type made by consumers in the literature is treatment decisions. One study that does discuss consumer decision types specifically is (Broadstock & Michie, 2000). These authors identified the following consumer medical decisions: when to consult a health professional; what assessment or treatment to undergo; whether to comply with a chosen treatment regime; and when and how to change their lifestyle. Each of these decisions may also pertain to decisions surrounding ADRs, in particular the first three. The fourth decision about lifestyle is peripherally related. A consumer may decide, for example, to alter diet in order to manage hypertension, which may result in a no treatment decision.

A list of decision-makers and the decision types made by these decision-makers that have been documented in the literature have been illustrated in Table 2-3. As can be seen from this table,

there is a limited understanding of the decision types made by decision-makers within the ADR decision domain, especially when compared with the decision types identified in the preliminary background work. Another important factor in understanding the requirements for decision support is developing an understanding of the decision types made by each decision-maker, and determining which of these decisions, if any, would benefit from decision support.

	Consumer	Medical Practitioner	ADR Expert	Pharmacist
Detecting and Diagnosing		X	X	
Treatment	X	X		
Prescribing		X		
Reporting	X	X		X
Seek treatment (Broadstock & Michie, 2000)	X			X
Lifestyle decisions (Broadstock & Michie, 2000)	X			X

Table 2-3 Decision types made by each decision-maker

2.3.4. ADR DECISION ENVIRONMENT

Each decision made has a context, and characteristics that define it, for example, a decision or set of decisions may have a time dimension. Time may be unlimited, such as the decision about which coffee machine to purchase, versus very limited time such as navigating a fighter plane in a conflict situation. The dimension may alter according to certain parameters, such as in the situation with a fighter pilot, the time to make a decision is likely to alter according to whether the plane is stationary, flying a routine flight, or in combat.

The following characteristics of the ADR decision environment emerged from further analysis of the data collected in the preliminary background work of this thesis. The characteristics of the ADR decision environment depend on whether the decision is made by a single decision-maker, multiple single decision-makers making decisions in isolation, or a collaborative decision or set of decisions. The analysis of current ADR decision support systems indicates that ADR decisions are primarily individual decisions. The description of medical practitioner/consumer

decision models (section 2.3.6) suggests that medical decisions may also include various levels of collaboration. It is assumed for the moment, that the set of decisions surrounding an ADR may be single decisions by a consumer or medical practitioner, or collaborative decisions.

These domain characteristics are described in the following sections.

2.3.4.1. Decision-maker characteristics

Medical practitioners:

- are novice to experienced (new graduates to experienced specialists);
- each have a different body of knowledge of medications and their potential ADRs. Each medical practitioner has a set of medications s/he is more familiar with than other medications. (a specialist may prescribe a drug and have a set of regular medications, a general practitioner may have a different set of familiar medications, a consumer may be being treated by the general practitioner, but taking a medication prescribed by a specialist);
- vary in use of computers from full electronic consumer records to fully manual consumer records.

Consumers:

- are medically untrained in most cases, however they may know more about their disease than a medical practitioner, especially if they have a chronic disease;
- have varying access to information, from limited access to information to sophisticated skills in accessing the Internet.

2.3.4.2. Decision characteristics

ADR decisions:

- require unique form of diagnosis. In many cases they appear to be random, unpredictable and sparse;
- a decision support system may assist with decision-making, but the decision needs to remain with the person making the decision. (A tool needs to augment rather than replace decision-making);

- the decisions include risk, some that have been identified, and some risk factors that have not been identified;
- the need to make a decision may not be identified. A reaction may not be recognised by the consumer and or the medical practitioner as a drug reaction, but attribute the symptoms to a disease;
- the differential diagnostic decision between an ADR, pre-existing disease or new disease may not result in a decision of 100% certainty. The decision is likely to remain at a lower level of certainty and may be revised over time;
- the decision is dynamic in nature. The consumer's symptoms are likely to change over time and test results will be available at varying times;
- the prescriber may not get feedback. The consumer may not seek treatment, or may seek treatment at another clinic for a suspected ADR.

2.3.4.3. Environment characteristics

In the ADR decision environment:

- a medical staff member may have limited time. A consumer may have more time to think about the problem;
- information must be able to be accessed very quickly;
- medical staff are generally not required to provide an argument for their decision, but may be challenged by a consumer or administrator (in contrast with legal decisions);
- no preparation time available in many cases;
- the level of risk associated with an ADR varies from minimal to highly significant.

2.3.4.4. Information and knowledge characteristics

Information can be defined as knowledge that has been obtained from investigation, study or through instruction (Merriam-Webster, 2003). Knowledge can be defined as knowing something, having familiarity that has been gained by experience and that is within a person's range of information (Sykes, 1976). Based on these definitions, it appears that information is what is transferred between people, and knowledge is what is understood from one or more sources of information by a particular individual. Just because information is given to a person, it does not mean it automatically becomes knowledge. The person receiving the information

may not agree with the information, or perhaps may not understand the information. It seems reasonable to conclude, therefore, that information received must be integrated with current knowledge in order to become new knowledge.

Information characteristics identified include the following:

- the source of ADR information needs to be clear to the prescriber;
- the applicability of ADR information used to make ADR decisions needs to be specific to the consumer;
- past history information needs to be accessible to the decision-makers;
- there can be uncertainty about the accuracy of some of the available information used to make the decisions;
- the consumer may have a medical history that contains individual risk factors but they may be lost in a large hand written medical file, various components of the record may be in different locations, the information may not be easily accessible to the medical practitioner and consumer in the short time frame available;
- critical information may not have been included or highlighted in the medical history.

Knowledge characteristics identified include the following:

- differing opinions between medical staff on the definition of an ADR versus side-effect;
- differing opinions on the severity of ADRs;
- that decisions are made with incomplete knowledge. Decision-makers inability to realise they are working with partial knowledge;
- may involve negative knowledge: that is, the symptoms may not match to a diagnosis the decision-maker is familiar with. The decision-maker, therefore knows the diagnosis has to be from the set of diagnoses s/he has not seen previously.

An understanding of the decision domain will assist in determining which tools would be most appropriate when developing decision support. An aim of this thesis is to develop, further, this understanding of the ADR decision domain.

2.3.5. DECISION THEORIES AND TECHNOLOGIES USED IN DECISION SUPPORT APPLICATIONS

Understanding the ADR decision domain and an understanding of how decision-makers currently make ADR decisions will assist in matching these decision processes to current decision theory. Knowledge of the decision theories that are used within this domain may then assist in choosing technology that supports the underlying theory. The literature does not neatly fall into the building blocks suggested in Figure 2-1. Theories of decision-making such as Utility Theory, have been described in the decision theory literature. Some techniques that have been described within the decision support literature, such as case-based reasoning, are based on assumptions about human decision-making, but do not rely on formal decision theory or models of decision-making. These theories and techniques, therefore, have been grouped together in this one section, to describe an array of methods of supporting decisions.

Carroll and Johnson (1990) classify decision theory into the following categories:

- **Descriptive** – how humans do make decisions currently – with their limitations
- **Prescriptive** – how humans 'should' make decisions if decisions are to be effective and well thought out.
- **Predictive** – how to predict the decisions humans are likely to make based on their individual preferences.

These categories are useful when clarifying the role of the decision support to be considered. Is the nature of the decision support to replicate human decisions, prescribe how humans could make 'better' decisions, and/or access information from experts that can be used to predict future decisions, providing support for non-experts.

2.3.5.1. Cognitive Theory

Cognitive research about human decision-making says that humans cannot make complex decisions based on some human limitations. These are things such as attention, memory and arithmetic calculations (Carroll & Johnson, 1990).

Attention

Humans have selective attention. They attend to things they see as important – not all information, and not necessarily all relevant information (Carroll & Johnson, 1990).

Memory

According to Carroll and Johnson, (1990), humans have a finite number of chunks of information they can attend to at any point in time. Thorough decision-making may require more information to be retained for all possible solutions to be considered, and all of the knowledge required to make an appropriate decision. Humans therefore make short cuts such as:

- making decisions based on past decisions;
- choosing the information they see as key information and ignoring the rest;
- choosing information based on a bias and ignoring the rest;
- framing the problem in a particular way which biases the information.

A set of decision theories that have been developed to assist humans with some of their cognitive limitations is discussed in the following section.

2.3.5.2. Clinical decision-making theories

Until about 40 years ago, it was assumed that medical education, continuing education, journals, individual experience and exposure to colleagues was enough to ensure medical decisions were of a high quality. According to Eddy (2005), in the 1970s there was a growing body of evidence to suggest that individual medical practitioners were making different decisions for similar problems, and after significant decision analysis, the conclusion was that it is not possible for anyone to accurately process all of the information needed for complex medical decisions (Eddy, 2005), a conclusion in line with the cognitive issues described in the previous section. A second problem was that there was a gap between clinical research and what was happening in clinical practice. Two methods of addressing this gap emerged: evidence based guidelines and

evidence based individual decision-making. Eddy (2005) discussed the need to combine these methods to support clinical reasoning.

Eddy (2005) described evidence based guidelines as having the following four characteristics:

> First, in all of them the work of analyzing the evidence and developing a guideline or other policy is done by small groups of specially trained people, usually sponsored by an organization. Second, they all use an explicit, rigorous process. Third for all of them the "product" – whether it be an evidence review, a guideline, or another type of policy – is generic. It is intended to apply to a class or group of patients defined by some clinical criteria, rather than to an individual patient. Fourth, their effects on care are indirect. That is, they are intended to enable, guide, motivate, or sometimes force physicians and other types of providers to deliver certain types of care to people, they do not directly determine the care provided to a particular patient (p. 13).

The focus for evidence based individual decision-making is "on educating physicians to help them bring more research and evidence into their individual decisions about individual patients" (p. 14). Clinical based guidelines were discussed in detail in section 2.2.5.3.

Differential diagnosis

One of the decision types described in section 2.3.3 was differential diagnosis. There are two principal methods of clinical decision-making that are discussed in the literature that relate specifically to differential diagnosis: making a diagnosis by selecting a hypothesis (hypothetico deductive reasoning); and pattern recognition or pattern matching. Each of these methods have strengths and weaknesses that will be reviewed in the following section.

Diagnosis as selecting a hypothesis

One strategy for making a diagnosis is by selecting a preferred diagnosis from a number of hypotheses, a process which is also referred to as hypothetico-deductive analysis (Elstein & Schwarz, 2002). Diagnosis is made by selecting a number of hypotheses. "Each hypothesis can then be used to predict what additional findings ought to be present if it were true, and the diagnostic process is a guided search for these findings" (p. 729). Methods such as Utility

Theory (described in section 2.3.5.3), rely on the weighting of each hypothesis based on new evidence.

Elstein and Schwarz (2002) found that this method is used by novices and experts, however the experts were able to process the information faster. They stated that it is possible to collect data thoroughly, but ignore, misinterpret or misunderstand some of the findings. Decision-makers may also fail to collect enough data, but interpret what they do collect accurately.

Pattern recognition

A second method of diagnostic reasoning is pattern recognition (Elstein & Schwarz, 2002). Pattern recognition relies heavily on a well-organised store of knowledge and the ability to recognise new problems in terms of older familiar problems previously dealt with (Crook, 2001). Experts who are in familiar situations with cases they see frequently may not regularly use a hypothetico-deductive reasoning method, however they may revert to this method for complex cases. Instead they use automatic retrieval. An old case is retrieved based on memory of a case with similar characteristics. Pattern recognition is now acknowledged as a central feature of expert performance (O'Neill, Dluhy & Chin, 2005).

A variation of the pattern recognition theory of diagnostic decision-making is Donald Schon's theory of reflection-in and reflection-on-action (Smith, 2001). Schon describes this reflective process using past situations to inform new situations.

> When a practitioner makes sense of a situation he perceives to be unique, he sees it as something already present in his repertoire. To see *this* site as *that* one is not to subsume the first under a familiar category or rule. It is, rather, to see the unfamiliar, unique situation as both similar to and different from the familiar one, without first being able to say similar or different with respect to what. The familiar situation functions as a precedent, or a metaphor, or…an exemplar for the unfamiliar one (Schon 1983: 138, cited by Smith, 2001).

The key difference in Schon's theory is that there is a time of reflection prior to selection of past cases, and the concept of choosing a past case or situation that does not have to be the same as the current situation, just have some elements that are similar.

Another issue highlighted by Crook (2001) is that when psychiatric nurses are required to make decisions in high risk situations, their experience appears to take in a holistic approach which includes the 'nature of knowing'. Crook's (2001) belief is that this 'knowing' is based on significant experience, but as yet is not well understood, and cannot be accounted for by current decision-making theories. The concern he highlighted is that with the increased emphasis on evidence to inform practice, the skills being used by experts may be lost to more formal and quantifiable methods. This concern has been expressed in articles which criticize this method stating that clinicians may make a diagnosis based on a past pattern which is incorrect. Making a firm diagnosis too early, may result in ignoring symptoms that point to a different diagnosis (Hamilton, 2004).

Complexities and need for flexibility in the use of diagnostic decision making

Diagnostic decision-making in health may include: serious and complex issues; two or more mutually exclusive actions from which to choose; significant risks and benefits; uncertainty about the likelihood that risks and benefits will occur in certain situations; no clear-cut choice; personal preferences and/or values for each choice, with multiple decision-makers; requires time to weigh up the risks and benefits to make a decision (Narayan, Corcoran-Perry, Drew, Hoyman & Lewis, 2003).

Clinicians alter the diagnostic decision-making strategy used depending on the individual case (O'Neill et al., 2005). This appears to depend on the experience of the clinician and the complexity of the case (Elstein & Schwarz, 2002; O'Neill et al., 2005). O'Neill et al,. (2005) developed a model of novice nursing decision-making that involves checking for past case information, and either using it as a starting point in the diagnosis, or if there is no case information, commencing with a hypothetico-deductive reasoning process. They also stated that a limitation of their model is that it is linear, whereas clinical decision-making often has components that are serial, dynamic, and overlapping in nature.

It is clear from this literature, that any decision theories attempting to explain medical diagnostic decision-making need to incorporate a set of complex, parallel and competing factors where there is often risk, uncertainty. In cases where there are multiple decision-makers there is a need to reconcile individual preferences, values and beliefs in a context which is dynamic and time constrained. A combination of methods is likely to be required for any diagnostic decision-support system.

2.3.5.3. Utility, Expected Utility Theory and Multi-attribute Utility Theory

Some decision theories commonly used within the areas of decision support are Utility Theory, expected Utility Theory and multi-attribute Utility Theory. A brief introduction to each of these theories has been included in this section, and will be followed with an explanation of how they may be applied within the ADR decision domain.

Utility Theory

Utility theory is a decision theory that attempts to prescribe a method of decision-making to improve decision-making effectiveness. It states that decision-making can be assisted by determining human preferences, weighting those preferences and then assisting humans with decision-making based on those preferences (Taylor, 2000).

Each of, Utility theory, expected Utility Theory and multi attribute Utility Theory, are based on cognitive theory, and assume that decision-making is a cognitive process that can be articulated. They attempt to overcome some of the limitations described in cognitive theory, described in section 2.3.5.1.

Utility Theory can also be used as a statistical method for determining preferences (Bankhead 1999). In the study reported by Bankhead (1999), utility statistics were used to determine consumer preferences for treatment and compare these preferences with factors within their history such as prior experience of the treatment options.

Expected Utility Theory

Once utilities have been determined, predictions can be made using Expected Utility Theory (EUT). This theory is therefore a predictive decision-making theory. These can then be compared with actual decisions, and when utilities are made from experts, predicted decisions can be used as an expert system (Bankhead, 1999).

Multi Attribute Utility Theory

Multi Attribute Utility Theory (MAUT) is a method of eliciting and modelling knowledge from experts and making it available to non-experts. MAUT can assist particularly when there are multiple conflicting criteria (Mussi, 1999). Entities which represent real world objects are identified. Each entity has a number of attributes or characteristics. Independent attributes need to be identified. Experts of a particular domain are used to elicit weights of attributes, which reflect the relative importance of each attribute. The weights can be compared, which results in a choice, or recommended choice. By modelling expert choices, a decision aid can be developed which can then be available for non-experts.

Brennan and Anthony (2000) used MAUT to elicit entities, attributes and preferences from a group of expert nurses. The aim was to create an expert model of a nursing practice model, which they based on the manner in which nurses accomplish clinical goals. The aim of this study was to develop a model that could be used for benchmarking rather than to assist in decision support. The model could, however, be used to assist non-expert nurses determine priorities when developing a nursing practice.

Limitations of Utility Theory, EUT and MAUT

As stated, this group of theories, assumes that the weighting of preferences is a conscious cognitive task, and that the weightings are consistent between cases, and are accessible. One problem of this method is eliciting the respective weights for each preference from experts.

To assist with the difficulty in eliciting knowledge from experts, Mussi (1999) used a medical diagnosis example to propose an alternative method of eliciting weights. Rather than asking the experts to state their preferences, Mussi (1999) elicited preferences by studying case examples. The domain used within this study was expert's choice between two alternative tests in order to

make a medical diagnosis. The conflicting criteria were 'more is better than less' referring to effectiveness of a particular test, compared with the other issue of 'less is better than more' referring to attributes such as risk or cost. Mussi (1999) developed a method of automatically eliciting the weights based on the case examples.

Another limitation of these theories is the assumption that medical decision-making, either follows, or would benefit from following a linear, cognitive model of decision-making. The fundamental assumption, that experts either consciously or unconsciously weight preferences, may be true for some types of decisions, and not other types of decisions. Novice decision-makers, people learning how to consciously make decisions, may be more likely to use these methods. Experienced decision-makers may 'know' how to solve a problem, based on years of solving the same types of problems, but may not be able to access this knowledge. The assumption behind this theory is that experts continue to weight preferences, but do so using a higher cognitive level and so no longer have access to it consciously. Other theories of decision-making may explain the behaviour of experts more effectively.

Application of Utility Theory, EUT and MAUT to the field of ADRs

Decisions surrounding ADRs have multiple conflicting criteria, such as comparing the risks associated with taking a medication and the benefits of taking the medication, and the risks of not treating the medical condition. ADRs also have the characteristic that there are people with expert knowledge surrounding ADR diagnosis, however many medical practitioners such as general practitioners, although experts in medicine, may not have expert knowledge of particular ADRs.

Using MAUT to elicit important attributes and weights from experts may assist medical practitioners with differential diagnosis between ADRs and pre-existing diseases.

An advantage of using these techniques within the ADR decision domain may be that decision-makers are forced to think about their preferences and give careful consideration to their weights. They then have a clearer understanding of their own preferences and make utility assessment explicit (Taylor, 2000.). Once they have a clear understanding, this enables them to communicate their preferences more effectively. Comparisons between decision-makers can

highlight disagreements so they can be discussed. Given the time constraints of the ADR domain, this approach may not be practical.

The additional complexities with the ADR domain include the dynamic nature of the decision domain, and in particular the increasing awareness that the decision domain is a collaborative domain rather than a single decision domain. Each incident of a suspected ADR will have different circumstances surrounding it, including different pre-existing diseases, symptoms and groups of symptoms that vary from consumer to consumer. Symptoms throughout the course of a diagnostic process change with time. Knowledge of ADR decisions is constantly increasing through processes such as spontaneous reporting. Knowledge of disease is also increasing. Developing an expert system about ADRs using MAUT would require significant maintenance to update the knowledge, and relies on the assumption that accessing reliable weightings from experts is possible. This group of theories may provide a contribution to this problem, but on their own are unlikely to provide a solution.

2.3.5.4. Rule-based systems

A detailed account of the history of diagnostic systems can be found in Miller and Giessbuhler (1999). Clinical decision support systems can be broad general systems, or systems that are specific to a narrow domain. According to Miller and Giessbuhler (1999), a large number of rule-based systems exist, and most have been applied to a narrow domain, due to the extreme complexity of maintaining systems with more than a few thousand rules.

The early systems had the goal of replacing the clinician. According to Miller and Giessbuhler (1999), this style of system was abandoned in the 1980s, and the focus moved more towards the development of systems that assisted the clinician make diagnoses, rather than make the diagnosis for him/her. They state that issues with the broad based systems include ensuring the system is updated to include new knowledge, however it is difficult to know when new knowledge becomes fact and the problem with the narrow domain systems is that medical practitioners and hospitals may not choose to spend large amounts of money on multiple narrow systems.

An early attempt at developing an expert medical system was MYCIN. (Cendrowska & Bramer) MYCIN is a rule-based expert system that was developed by Edward Shortliffe in the 1970s at the Stanford Medical School. It was designed to assist physicians with diagnostic and treatment decisions caused by certain kinds of bacterial infection. This system interacted with physicians collecting information about specific consumers, by conducting an interactive dialogue with the physician. If further information was required throughout the process, the system would attempt to infer it, or ask further questions. Once a reasonable diagnosis could be made, MYCIN would provide the diagnosis and then a list of possible treatment alternatives. Even at this early stage in expert software development, MYCIN had the ability to reason with uncertain information.

This system had some features designed to increase its acceptability to physicians. It was easy to use, tolerant of spelling errors, and could recognise synonyms. It was easy to update the rules, and at the end of the consultation provided an explanation of the decision. If an expert felt a rule was incomplete or incorrect, s/he was able to update the rule set.

Cendrowska and Bramer (1984) reconstructed the MYCIN system in order to understand its processes and to critically evaluate it. Problems identified included internal integrity problems resulting in inconsistency in decision-making. This appeared to stem from the statistical methods used to manage the uncertain information. MYCIN did, however contribute to many issues such as acceptability by an end user group, managed interaction and provided transparency of its decision process by providing an explanation of the decision, as well as making decisions within a specific domain.

The main problem with rule-based systems is that they require a set of rules that have been elicited from a group of experts, but are static in nature, and cannot manage dynamic situations. As new knowledge is discovered, the rules need to be updated, which can be a time consuming process. They also generally do not manage uncertain information well.

The ADR domain is one where the knowledge base is constantly changing and where the information is uncertain and incomplete. Rule-based systems have been built for use within hospital settings where consumers are being monitored and there are rules about the acceptable

range within factors such as blood pressure and the results of liver function tests. These systems are generally limited to a small set of inputs, and diagnose a limited set of ADRs. In this domain, the system monitors what is normal, and if the readings become anything other than normal, an alert is triggered.

Rule-based systems do not respond to a dynamic environment. As previously discussed, there are many factors within the ADR decision environment that are dynamic. There is no clear set of rules that clearly define when a set of symptoms is more likely or less likely to be an ADR.

Like the Utility Theories, a rule-based decision support system is unlikely to be a feasible solution to the issue of ADRs, but may be useful for a component of the domain, as has already been suggested and implemented in hospital clinical systems.

2.3.5.5. Case-based Reasoning

Case-based reasoning is a method of solving new problems by accessing a database of old problems. In the case of ADRs, ADRs that have been previously documented in *The Australian Adverse Drug Reaction Bulletin* are cases that have occurred in the past that have a particular diagnosis attached to them by ADRAC.

Case-based reasoning could be used for differential diagnosis, by creating a database of previously diagnosed cases. One source of these cases may be *The Australian Adverse Drug Reaction Bulletin*. *The Australian Adverse Drug Reaction Bulletin* is an example of particularly interesting or unusual cases. In order to develop a database of case studies of the less common ADRs, medical practitioners in areas of specialty who see particular types of ADRs on a regular basis could recall either individual cases, or a typical case, describing the key characteristics of that typical case. These cases could then be stored in a database for other's to access.

The cases could sit in a repository that could be accessed when a medical practitioner or consumer requests access to the database. A more effective solution, however, may be one where the cases database sits in the background, but when the medical practitioner or consumer inputs symptoms and consumer characteristics, the case-based reasoner searches for identical or

similar cases, and if one or more are found, indicate to the decision-makers that these cases have been found ready to be referred to if required.

At this stage, an ADR diagnostic decision model, or a set of rules for diagnosis has not been found within the literature, which makes this domain less conducive to a rule-based system. Also, the knowledge base is constantly changing. There are new drugs on the market, and there are newly recognised ADRs regularly being documented. Updating a rule-based system to reflect these changes would be a significant task, whereas adding new cases to the case database and distributing it, would be far less time consuming.

A database of past cases does exist in the form of *The Australian Adverse Drug Reaction Bulletins*, and although an ADR may be a novel diagnosis to one medical practitioner, across medical practitioners it is not a novel problem. Previously undocumented ADRs would obviously not be included within the case database, however, the absence of a diagnosis, followed by a suspicion of an ADR and temporal knowledge supporting this suspicion, may be enough for the medical practitioner to report the suspected ADR to ADRAC. If enough medical practitioners do this, either within Australia or across the world, a new case can be developed which could then be added to the database.

Main, Dillon and Shiu (2001), in their tutorial on case-based reasoning refer to several components of a case-based reasoner. There is the database of cases, a problem case, a case retriever, a case reasoner, and then a derived solution. The case retriever searches for identical cases within the database of cases. If no identical case is found, the database searches for similar cases. The case reasoner then attempts to adapt the similar case in order to derive a new solution.

If the view is taken that decision support is most powerful if computers do the tasks that humans find difficult, but allow humans to do the tasks they do well, it would seem reasonable that within the ADR context, searching for identical or similar cases, and the storage and indexing of cases is something a computer would do well. The task of looking at a similar case and matching key attributes to the problem case, and determining quickly if the same diagnosis

would apply to this new case, is something a human would do well. The case reasoner, therefore, may not be a required component within this domain.

According to Main et al. (2001), a case-based reasoner may develop new cases based on adapting old cases. These new cases then need to be tested in the real world. Using the ADR domain, new cases, hypothesised by the ADR decision-makers could be tested by submitting the new cases to ADRAC. ADRAC would then verify or otherwise the 'correctness' of the new case, and determine if it were to be added to the database. If anyone were to update the database, there would be a risk that the integrity of the cases would be compromised.

2.3.5.6. Agent-based systems

Agents have been described by Majewski (1996) in Knapik and Johnson (1998) as having the following characteristics:

- **Autonomy**: Agents have the ability to operate without the direct intervention of humans or others. They have some kind of control over their internal state.
- **Social ability**: Agents can interact with other agents and/or humans via an agent communication language.
- **Reactivity**: Agents can perceive their environment. They can respond in a timely fashion to changes that occur in it.
- **Proactivity**: Agents do not simply act in response to their environments, but are also able to exhibit goal-directed behaviour and can take the initiative.

Jennings and Wooldridge (1998) define agents as being "a computer system situated in some environment and is capable of autonomous action in this environment in order to meet its design objectives" (p. 4).

Multi-Agents

Multi-Agent Systems (MAS) can be seen as a group of entities interacting to achieve individual or collective goals (Barber, Han & Liu, 2000). Agents can have additional characteristics

according to the application requirements. Some characteristics that have been described in the literature include the following:

Co-operation

Agents can co-operate to solve problems that individual agents may not be able to solve. In order to do this they need to know other agent traits or current status via inter-agent communication. Tasks will be assigned based on this information (Katoh, Kinoshita & Shiratori, 2000).

Coordination

Co-ordination techniques may include negotiation, arbitration, voting and self-modification. Barber et al. (2000) describe the following coordination techniques.

- **Negotiation** – assumes agents are rational and intelligent so they consistently manage their goals. They aim for the highest payoff, measured by utilities.
- **Arbitration** – a third party makes the final decision when a conflict arises.
- **Voting** – based on the human experience of voting.
- **Self-modification** – a technique used when agents do not want to interact with other agents.

Risk and Uncertainty

Agents can be designed to work in conditions of risk and uncertainty. Methods such as probability and utility, from decision theory, can assist in dealing with uncertainty. A utility can be assigned to a belief factor of how certain the agent feels the information may be (Russell & Norvig 1994, in Knapik & Johnson 1998).

Adjustable autonomy

A recent expansion of agent ability has been the concept of adjustable autonomy. Scerri, Pynadath and Tambe (2004) developed a method of adjusting the level of autonomy that an

agent used. When necessary, the agent would transfer control of a task to a human, other times working in the background.

ISAs (Intelligent software agents) have been used in a number of domains. The two that most closely align with the goals of this work are medical applications and applications for information management.

ISAs can be used in medical applications for patient monitoring. This may be in an intensive care unit where frequent readings can be made and interpreted. Multiple agents may be working as an intensive care unit team. Each ISA may have the responsibility for some component of the management of the consumer. They need to co-operate, negotiate, compromise and work together for the overall benefit of the consumer. If necessary, ISAs can then alert medical staff for their intervention (Haynes – Roth et al. 1989 in Jennings and Woodridge 1998).

ISA systems have been developed in the domain of information management, for filtering and gathering information that is stored on the world wide web.

Amalthaea from the MIT media laboratory is a multiagent system that discovers, monitors and filters information. The basis of this system is that people have overlapping and competing interests. Their preferences change over time. Their system is a society of agents that monitor for new information, determine the information that fits within the person's preferences. Over time the person may change their preferences. Systems such as this would modify their search criteria based on these different purposes.

ISAs assist in solving complex problems, and therefore might be useful within the ADR domain. As discussed, ADR decision-making involves multiple decision-makers, each decision-maker with varying amounts of knowledge, different beliefs and goals. They have the shared goal of avoiding harm from drug therapy, and maximizing the consumer's health.

It is not feasible for agents to replace decision-makers due to the constant change in priorities, symptoms and information sources; however they may have a role in augmenting information

sharing and decision-making by sitting between the decision-makers. It may be possible to use a single agent, or an agent may represent each of the parties.

2.3.5.7. Argumentation

Argumentation is particularly concerned with domains which include argumentative discussion, persuasion dialogue or critical discussion. In particular situations where there is a difference of opinion, conflict or dispute (Norman, Carbogim, Krabbe & Walton, 2003).

The ADR decision domain is less about resolving a conflict, and more about obtaining a shared goal of a feasible diagnosis, or a treatment option that is satisfactory to each party involved. The decision-makers generally are not adversarial, but co-operative.

An assumption underlying the classical methods of representation and reasoning is that the information is complete, certain and consistent. Argumentation is a method that uses the inconsistency to offer insights into rational processes, by using imperfect information by constructing and weighing up arguments relevant to alternative conflicting conclusions (Carbogim, Robertson & Lee, 2000). The ADR decision domain, like most medical decision domains has incomplete and uncertain information.

Girle, Hitchcock, McBurney and Verheij (2003) discuss the decision domain of asking an expert for advice to assist with decision-making, a domain characteristic that is more in line with ADR decision-making. They state that:

> When faced with difficult decisions about what to do, decision-makers benefit from good advice. Good advice comes most reliably from advisors with relevant expertise. As well, good advice has at least three other essential features. First the advice should be presented in a form which can be readily understood by the decision-maker. Second there should be ready access to both the information and the thinking that underpins the advice. Third, if decision-making involves details which are at all unusual, the decision-maker needs to be able to discuss those details with her advisors (p. 56).

The idea of explanation, rather than argumentation, is more in line with the ADR domain. Explanation of reasoning, when two or more parties are attempting to come to a joint mutually

beneficial decision, can assist in joint understanding. It also can lead to clarification of an idea, and it can allow another person with a different set of knowledge, to point out inconsistencies, or additional information that needs to be used in order to make the decision.

Shared decision-making between, in particular, the medical practitioner and the consumer involves each party having partial, and incomplete knowledge, each needs an understanding of the other's perspectives and reasoning in order to make a decision.

Given the fact that this is a co-operative decision domain, rather than putting resources into decision support to assist with sharing knowledge, preferences, beliefs, priorities, again, it may be more beneficial to train both groups of people in performing this task via conversation. In conflict situations, conversation is more difficult and so decision support may be more useful. In co-operative situations, education may assist in developing the skills that develop this level of shared decision-making.

2.3.5.8. Decision theories and the choice of theoretical framework

At the commencement of this work, a discussion took place about the use of the positivist theoretical perspective as the basis for the majority of ADR decision support, and decision support generally. This is also reflected in the decision theories, and decision support techniques that have been discussed above. In particular, theories such as Utility Theory, rule-based methods and to some extent case-based reasoning, are situated in the idea that knowledge is objective. Each of these methods attempts to find the most effective solution to a problem, based on a set of criteria for 'effective'.

This work has been based in the area of social constructionism. This shifts one of the basic assumptions of decision support. Rather than attempting to find the most reliable and consistent objective solution, an attempt is being made to reconcile the perspectives of a number of decision-makers. Each of these decision-makers will have their own understanding, preferences and priorities of the factors within the problem that are most important, to find a solution which is satisfactory to the decision-makers, and is likely to be unique to the case in question.

The last two techniques discussed, multi-agent technology and argumentation, may be applicable to decision support designed from a social constructionist perspective, as they each consider multiple individual perspectives and attempt to reconcile these.

2.3.6. DECISION MODELS

A set of models of decision-making that relates to this domain is Emanuel and Emanuel's (1992) medical practitioner/consumer decision-making models. These models have been discussed by a number of authors, and developed further by Charavell et al. (2001). A discussion of this model and it's application to this domain will be discussed in this section.

Clinical-decision-making models

Scott and Lenert (2000) discuss the issue of decision support systems for patients. They refer to four possible models of medical practitioner/consumer decision-making. Paternalistic; Informed, Collaborative, and Deliberative models were originally described by Emanuel and Emanuel (1992). Paternalistic decision-making is defined as a model where by the clinician has complete authority to make decisions on behalf of the consumer. Scott and Lenert (2000) stated that the proportion of consumers who prefer a Paternalistic model is three to eight percent. Informed decision-making is defined as a model whereby the consumer makes completely autonomous decisions. The role of the clinician is to provide medical information, but it is assumed that the consumer is responsible for determining their own preferences, and making the final decision. 20% to 30% of consumers preferred the Informed model. Collaborative decision-making is defined as a model where the consumer relies on the health provider to provide information, but also to facilitate the decision-making processes. 50% to 60% of consumers preferred the Collaborative model. The final model is described as Deliberative. In this model, the health provider attempts to convince the consumer of the best outcome for their health, based on what the medical practitioner believes is in the consumer's best interests. Ten to 20% of consumers prefer the deliberative model.

Scott and Lenert (2000) stated that although consumers may want to participate in medical decision-making, they have limitations such as education, numeracy, problem solving skills, and understanding their own preferences. They believe that there are two key ways to improve

consumer decision-making. Firstly to assist consumers with their limitations, and then to provide decision support that can accommodate multiple if not all of the clinical decision models.

Some authors in England have found that consumer participation in medical decision-making can have improved health benefits for the consumer (Stewart, Brown, Donner, McWhinney, Oates, Weston & Jordan, 2000; Stewart, Meredith, Brown & Galajda, 2000). The results from Stewart et al. (2000b) were that:

> Patient-centred communication was correlated with the patients' perceptions of finding common ground. In addition, positive perceptions were associated with better recovery from their discomfort and concern, better emotional health 2 months later, and fewer diagnostic tests and referrals (p. 796).

Stewart et al. (2000a) gave an example of how consumer involvement in decision-making assisted in improved outcomes:

> For example, concordance between patient and physician expectations and patient participation in the decision-making process affects older patients. Communication is also linked to patient recall, adherence, and satisfaction. Furthermore, communication impacts emotional and physical outcomes of older patients, although evidence of improved physical outcomes remains under-investigated in this population. Dimensions of communication, such as continuity of relationship, seem to be important in decreasing hospitalization of older patients (p. 25).

Charavell et al. (2001) also begin with Emanuel and Emanuel's (1992) models of decision-making. They see the paternalistic and informative models as reducing the exchange of information, where as the collaborative and deliberative models attempt to increase the exchange. They then suggest an alternative definition of shared decision-making, which sits between the collaborative and deliberative models. This shared decision-making model includes the physician conveying information about the condition, including risks and benefits of various options. The physician would elicit preferences from the consumer and assist in the decision-making process, and also state their own preferences for the consumer. Charavell et al. (2001)

state that although this appears to be a more effective model of decision-making it remains open to interpretation regarding how much each party contributes to the sharing of information.

Charavell et al. (2001) stated that physicians include information that consumers do not have, and that it is not until the information has been conveyed, and the risks and benefits have been weighed, can a consumer contribute to the decision-making process. In the domain of ADRs, the consumers also have information that the medical practitioners do not have access to, authors continually refer to consumer preferences, however consumers also have access to their history, their knowledge of their own bodies, and knowledge of past decisions they have made, all of which also need to be included in order to make informed decisions. This shared decision-making model could be expanded further to include the additional information available to consumers that needs to be exchanged to enhance ADR decision-making.

The idea that consumers use information other than the information perceived as key factors by the prescriber, is supported by a study by Benson and Britten (2002). These authors conducted a qualitative study to understand consumer decisions about whether or not to take antihypertensive medications. They concluded that consumer decisions may include preferences around issues other than the pharmacology of the drug, such as a desire to use a treatment other than drugs, a belief that drugs are signifiers of ill health, the consumer was brought up to avoid drugs, and a belief that medical practitioners prescribe drugs too readily. They stated that consumers make decisions in ways that make sense for them personally, and for medical practitioners to assist their consumer's to make informed decisions, they need to first understand the factors that the consumers perceive as important, factors which may not even be considered by the medical practitioner.

Another study on medical practitioner-consumer decision-making about drugs (Stevenson, Barry, Britten, Barber & Bradley, 2000) studied medical practitioner/consumer interactions in a clinical setting, and found little evidence that both medical practitioners and consumers participate in decision-making. This same group of authors in a different study (Britten, Stevenson, Barry, Barber & Bradley, 2000) investigated misunderstandings in prescribing decisions. They identified 14 categories of misunderstandings including patient information unknown to the medical practitioner, medical practitioner information unknown to the patient,

conflicting information, disagreement about attribution of side effects, failure of communication about medical practitioner's decision, and relationship factors. They stated that all misunderstandings were related to a lack of consumer participation in the consultation, and they were all associated with either potential or actual adverse outcomes.

Another group of authors recognised that for shared decision-making to be a realistic option, medical practitioners need training (Towle & Godolphin, 1999). A set of competencies required by medical practitioners to engage in shared decision-making include: development of a partnership with the consumer; establish consumer's preferences; review the consumer's preferences and determine their level of certainty; ascertain and respond to the consumers ideas and/or concerns; identify choices; provide evidence to support each choice and help the consumer reflect on the options available to them, negotiate a decision; and agree to a plan. The competencies identified that are needed by a consumer include: defining a preferred doctor-consumer relationship; find a medical practitioner and develop a partnership; identify own health problems, feelings, beliefs and expectations; communicate these factors to the medical practitioner; access information; evaluate information; and negotiate decisions.

As discussed in section 2.2.5, drug surveillance programs, and providing information about drugs, the pharmacology of drugs, drug interactions, guidelines about drugs, contra-indications etc, are all about providing evidence to the prescriber at the time of prescribing. The preliminary background studies (O'Brien & Yearwood, 2002) indicate that decision-making processes surrounding ADRs may be a contributing factor to the incidence of ADRs, an idea which is supported by Britten et al. (2000). As stated previously, misunderstandings were associated with adverse outcomes, and training in shared decision-making competencies is an important component.

2.4. The use of grounded theory to analyse case studies in systems engineering

Researchers in the Information Systems (IS) domain, have been exploring the usefulness of qualitative methods in their domain for the past two decades:

> In Information Systems (IS), there has been a general shift in IS research away from technological to managerial and organizational issues, hence an increasing interest in the application of qualitative research methods (Myers, 2004, Introduction section, para. 1).

The problem of gathering the requirements before building software or developing information systems, is ongoing. Alvarez and Urla (2002) emphasise this point:

> A plethora of approaches have been developed over the last few decades to improve the quality of information elicited from users during requirements analysis. IS researchers have spent a great deal of time comprehensively reviewing requirements analysis methods (p. 39).

Another group of authors state that one rationale for this is that "Incomplete and inconsistent requirements are a major cause of the failure of computer based projects" (p. 1) (Richards, Boettger & Britt Fure, 2002).

Three papers have been described below that discuss the use of grounded theory to analyse case study data to inform either the requirements analysis phase of systems design, or the processes used by information systems analysts to gather requirements analyses. Grounded theory is explained in detail in section 3.4.

Hughes and Wood-Harper (1999) investigated the use of grounded theory to analyse two organisational case studies as a component of the requirements analysis phase of systems design. The first case study was a three site veterinary practice. They used Miles and Huberman's (1994), modified form of grounded theory, beginning with 'seed categories' as a focus to the interview questions. The categories were, "…understanding of job roles and responsibilities, decision-making processes and communication between the three sites" (p. 88).

Hughes and Wood-Harper (1999) found that the recommendations arising from the analysis that were given to management were acted upon with satisfactory results. Although the process yielded positive results, the time taken to interview, transcribe, code and categorise the data took what they described as excessive time.

In their second case study, a small manufacturing company, Hughes and Wood-Harper (1999) shortened the analysis process by using the NUDIST qualitative software package, and listening to each tape recording, but only transcribing components. Any themes that had already been saturated by previous interviews were not transcribed. They found that this adapted method was also successful in achieving the systems analysis goals and provided a satisfactory outcome for the organisation's management team.

Hughes and Wood-Harper (1999) state that the primary advantage of this method is that research and practice can be performed concurrently, producing research to develop new theory, at the same time as producing business outcomes.

Orlikowski (1993) used grounded theory to analyse case study data from two organizations that used CASE (computer assisted software engineering) tools over time. The paper presented the findings of a grounded theory study into the adoption and use of CASE tools, and developed a theoretical framework for conceptualizing this as a process of organizational change. Orlikowski (1993), unlike Hughes and Wood-Harper (1999), above, used this approach to investigate the usefulness of a methodology of gathering requirements, rather than using the grounded theory analysis of case studies as a method in the way Hughes and Wood-Harper (1999) did.

Bryant (2002), in his critique of grounded theory research, points out the strength of Orlikowski's work; in particular "its extensive detail and the ways in which the differing accounts of the two case studies illustrate general and specific aspects of the experiences of CASE tool introduction" (p. 8).

Goede and De Villiers (2003), like Orlikowski (1993), used grounded theory to investigate IS practitioner's thinking about IS methodologies in order to improve the quality of work conducted by IS practitioners. They define quality as "the finished artefact is used by the users to solve the problem intended to be solved and that it was developed within given budget and time constraints" (p. 208).

Information systems researchers refer to two levels of analysis, those that involve 'hard systems thinking' and those that involve 'soft systems thinking'.

2.4.1. HARD AND SOFT SYSTEMS THINKING

Bell, Cooper and Qureshi (2002), discuss the role of hard systems thinking and soft systems thinking in the area of software and/or systems design. Discussing the work of (Checkland, 1981), they said:

> …the distinguishing characteristic of all hard systems thinking is the belief that real world problems can be investigated in this way. It is argued that most hard methodologies are goal centred or goal oriented in that **they assume the problem i.e. 'the what' is given** for [a goal state]. For example, to build a product to meet certain requirements, the usual objective is to find the best way of building the product to meet the requirements, i.e. 'the how' (p. 61).

Bell et al. (2002) continue to say that they agree that this assumption of 'the what' is a significant limitation of hard systems thinking. They then talk about the importance of including soft systems thinking:

> When investigating social situations, systems theorists realized that the problem, i.e. 'the what', could not be assumed as a given. Stakeholders may have different views of what are the most important problems to be solved in order to improve the situation. Soft methodologies have emerged with the aim of attempting to assist in understanding the perspective of the stakeholder; leading it is hoped, to relevant improvements in the area of concern (p. 61).

Bell et al's (2002) discussion of the need for 'soft systems thinking' supports observations within this work that beginning with 'the what' pre-defined, as in the initial requirements analysis project conducted at the commencement of this work, left out some key features. These features were only revealed when considering 'the why' and the purpose of the software or system, which resulted in standing back and conducting an analysis of the decision domain, which then allows 'the what' to be more clearly defined.

2.5. Conclusion

Injury and illness arising from adverse events within the medical domain is a significant problem within Australia and around the world. One aspect of this problem, the occurrence of adverse drug reactions, is the focus of this work. This chapter has provided some background to the domain of adverse drug reactions.

Efforts to reduce the incidence of ADRs include drug surveillance systems, computerised clinical guidelines, electronic prescribing with ADR decision support modules, early warning hospital based systems, and methods to increase awareness and provide information and education to people within this domain.

Within Australia, there are a number of initiatives currently under development that will assist in providing the infrastructure required for the development of medical decision support in the future.

The second part of this chapter outlined some aspects of decision support that may be useful to consider when designing a decision support system. These include knowledge of who the decision-makers are, the decisions to be supported, the decision environment, decision theories, decision models and techniques and technologies that have been found useful within the field of decision support.

Although it is encouraging that significant effort is underway to address the problem of ADRs within Australia and around the world, when comparing current knowledge of the ADR decision domain, with knowledge of a domain that assists in the development of decision support, there are some gaps. There is significant knowledge about the mechanisms underlying ADRs, however, there is minimal understanding of how the information and knowledge within this domain is used by the decision-makers, who the ADR decision-makers are and the types of decisions they make. There is little understanding of how ADR decisions are made and the decision theories that may assist in explaining these decisions. Although there are many techniques for developing decision support within the literature, determining which techniques

would be most useful within this domain, requires an in-depth understanding of the decision environment.

The final section in this chapter was a discussion that relates to methodology. Literature was reviewed where authors have used a grounded theory approach to the analysis of case study data to assist in the development of information systems. These methods may be useful to assist in understanding the pre-requirements analysis phase of systems design within this domain, as they encourage collecting real world data, and performing an in-depth analysis, using a technique that encourages stepping back from pre-existing assumptions about the domain. Rather than beginning the systems analysis process with a scoped project in mind, stepping back and taking a fresh look at the domain, may result in a more complete understanding of this decision domain, which will provide fertile ground for specifying requirements for the development of an information system.

As will be explained in the following chapter, these methods will be expanded by moving from a positivist theoretical framework to a social constructionist view of knowledge, and a symbolic interactionist theoretical framework. This movement of theoretical position, in combination with the collection of case study data from multiple perspectives of a single instance of an ADR, may provide an understanding of the domain that assists in understanding the complexities of this domain, adding to the knowledge that can be used prior to specifying one or more solutions, as well as contributing to the overall understanding of the ADR decision domain.

CHAPTER THREE

The Research Process

3.1. Introduction

This chapter discusses the research processes followed and the underlying philosophical perspectives and theoretical perspectives that informed this work. This chapter is structured according to four stages of the research process described by Crotty (1998).

Crotty (1998) defines each of these stages as follows:

> *Methods*: the techniques or procedures used to gather and analyze data related to some research question or hypothesis.
>
> *Methodology*: the strategy, plan or action, process or design lying behind the choice and use of particular methods and linking the choice and use of methods to the desired outcomes.
>
> *Theoretical perspective*: the philosophical stance informing the methodology and thus providing a context for the process and grounding its logic and criteria.
>
> *Epistemology*: the theory of knowledge embedded in the theoretical perspective and thereby in the methodology (p. 3).

Rather than choosing a methodology, analysing the results using this methodology, and then describing the epistemology that informs the methodology, Crotty's (1998) approach encourages the analysis of the data through the combined views of the epistemology, theoretical framework and methodology.

Using this structure, the epistemology behind this work, social constructionism, is described in section 3.2, followed by the theoretical perspective of symbolic interactionism in section 3.3.

The methodology used within this work is grounded theory, which is described in section 3.4, and the methods are described in section 3.5. Due to the sensitive nature of the data collected, there were ethical considerations to be considered which have been described in section 3.6.

This work crosses multiple research communities: medicine; the requirements analysis end of information technology; health informatics; and sociology. One challenge, therefore, is to present this work so that it accommodates each of these audiences. For a designer of a clinical decision support system, the theory behind the methodology introduces a number of new concepts. For a reader well versed in qualitative methods, exploration of the arguments that exist within each of the philosophical and theoretical perspectives, and providing a detailed rationale for an approach is an essential element. Too much detail may be a barrier to a software designer or medical practitioner. Too little detail may be a barrier to a qualitative researcher.

The primary aim of this work was to add insight into the ADR decision domain to inform the pre-requirements analysis phase of decision support systems. The epistemology, theoretical framework and methodology used within this work were the theories chosen to inform the research questions. To accommodate a wide audience, this chapter provides an introduction to the concepts, followed by a more detailed discussion of the position taken. Although there are major arguments between schools of thought at each theoretical level, an exploration of these arguments has not been included.

The underlying epistemology of traditional scientific research is objectivism, with a positivist theoretical perspective. As a consequence, the majority of medical research, and previous research investigating ADRs, is conducted using these philosophical perspectives. The key characteristic of both objectivism and positivism is that knowledge can be discovered by studying an object or behaviour, with a significant level of impartiality or objectivity. Research of this type is often reported without explicitly stating the epistemology and theoretical perspective, because within the community of readers of this paradigm, these theoretical assumptions are a given.

Researchers in the social sciences, however, make explicit the theoretical perspective behind their work. They acknowledge objectivism as one theory of knowledge, but argue that other

theories of knowledge are just as valid. This process of making the epistemology and theoretical perspectives behind this work explicit has been used within this work.

As discussed in the introductory chapter, ADR decision support that has been developed from a positivist perspective is based on the understanding that the concepts behind the ADR decision domain have a single understanding for all decision-makers. ADR decision-making is primarily concerned with and focused on the decision domain of the medical practitioner and is generally directed towards one or two decisions within this decision domain. This single perspective that underpins current ADR decision support is based, on limited knowledge of the ADR decision domain.

Rather than using this traditional positivist theoretical perspective, this work has been based in the epistemology of social constructionism, and used a symbolic interactionist theoretical perspective. This philosophical perspective, which will be discussed in detail in sections 3.2 and 3.3, is that people belong to social groupings and that each group has an understanding of concepts within their environment and use symbols and language to label and share ideas about these concepts. Based on this view each group of decision-makers within the ADR decision domain will have different understandings of each of the key concepts. Three decision-makers from this domain have been interviewed, the consumers, medical practitioners and experts, with the aim of understanding the decision domain from these three perspectives. Considering these multiple perspectives is important when developing decision support for this domain.

In order to explore these multiple perspectives, and to gain additional insight into ADR decision domain to inform the requirements analysis phase of systems design, case studies have been collected from the perspectives of the consumer, medical practitioner and expert that focus on a single instance of an ADR. These case studies have been analysed using a grounded theory approach. The grounded theory approach was used so that pre-conceived ideas about the decision domain could be set aside, as much as possible, to allow new insights into this domain to emerge, that have been grounded within the data. The methodology of grounded theory and the methods surrounding the collection and analysis of the case studies are described in detail in sections 3.4 and 3.5.

This combined approach of using a different theoretical perspective, in combination with a grounded theory analysis of case studies has resulted in additional insight into the decision domain.

3.2. Epistemology – Social constructionism

Positivism, as stated in the previous section, is a theoretical perspective that comes from the epistemology of objectivism. This philosophy is that all knowledge is contained in an object, and it is the researcher's role to *discover* that knowledge about the object or entity. Interpretivism, which comes from subjectivism, is the view that all knowledge and understanding of objects and the world is *created* by the observer. This paradigm assumes knowledge is culturally derived and historically situated. Constructionism sits between these two views. Constructionism is the view that knowledge is constructed by the observer, about a particular object or entity. Social constructionism explains constructionism from a social context. The view is that an individual does not construct reality randomly, but that an individual is born into a social environment with rules, expectations and behaviours, that existed prior to the birth of the individual and which is used as a basis for the construction of the individual's understanding and knowledge of the world around him or her (Crotty, 1998).

George Herbert Mead, a philosopher and social psychologist described the differences between behaviouralism and understanding behaviour using a social context (Mead, 1934). Behaviouralism he described, as the study of humans and animals through behaviours observed by the researcher. The meaning of those behaviours is determined by the researcher. Mead (1934) discussed a limitation of the behaviouralist approach; that it is not possible to determine the inner thoughts of the person being studied. He believed that one approach that allows researchers to access the inner thoughts, begins with the understanding of society, and then seeks to interpret behaviours based on the meanings attributed to those behaviours by the society in which they belong.

The philosophy of social constructionism is that meaning is constructed by society, and is adopted by each of the members of that society. A set of behaviours may have a meaning within one society and the same set of behaviours may have a different meaning within another society.

Society can relate to any social grouping including a country, city, race, religion, organisation, role, or any combination of these.

Green (2000), whose work is based in the epistemology of social constructionism, illustrates this influence of society, in this case a profession, on the meaning of evidence based practice. The background to her work is the increased emphasis on evidence based practice within a multi-disciplinary team. One issue raised by Green, was that there was an underlying assumption that there was a single understanding of 'evidence'. She found, however, that each discipline had a different understanding of this concept:

> Rather than being a neutral tool used to inform decision-making, evidence was both constructed through professional practice and contributed to the construction of professional identity (p. 453).

Green (2000) recommended that in order to work within a multi-discipline decision environment, any effort to use evidence based practice requires acknowledgment that different groups understand these concepts in different ways, and explicit discussion of the core concepts within this domain; evidence, practice and knowledge is a required initial stage.

Another aspect of social constructionism is the influence a social group can exert on its members. An example of the impact of social construction on behaviour is the work conducted by Dick (2000). She studied the influence of the organisational culture of the police force on work related stress using a social constructionist epistemology. She performed a qualitative analysis on field notes of counselling sessions to understanding the beliefs the staff members placed on their experience of stress. She said that:

> …not only do these constructions influence the ways in which officers perceive themselves and their environments, but they also operate at the collective level to 'normalize' some emotional responses and 'pathologize' others… (p. 226).

In this example, the beliefs of the social group became the beliefs of the individuals who joined that group. Behaviour of the members enforced these concepts within its members. Some of

the beliefs identified in the participants that perpetuated the stress related to the incongruence between the organisational belief system and the individual's belief system. This work illustrates that not only are beliefs adopted by the participants within a group, they can be imposed by other members of the group, to maintain the group identity.

Within the ADR decision domain, an example of a concept that has meaning for one group and minimal meaning for another group is the word 'compliant'. As will be discussed further in section 5.3.4.2, the term 'compliant' was a term used by the medical practitioners, but was not used by the consumers. The term 'compliant' has meaning within the language of medical practitioners and some other health professionals. This word, not only is a construct of the medical community, it implies the person using this word has a particular understanding of the respective roles of the medical practitioner and consumer. It implies that the medical practitioner has the role of recommending a treatment (possibly following a discussion with the consumer about their preferences), and the role of the consumer is to 'comply' with that recommendation.

In the same way that Green (2000) found that different professionals working together have a different understanding of 'evidence', it is the expectation of the researchers that the medical practitioner is likely to have different meanings for some of the core ADR concepts to that of either an expert, or a consumer.

It is from a social constructionism perspective that the data within this thesis will be interpreted. This will allow the meaning of the concepts within the ADR decision domain to be understood from a group and individual level. It is expected that the result will be a richer understanding of this domain by embracing the multiple understandings of the underlying concepts.

3.3. Theoretical perspective – Symbolic interactionism

Symbolic interactionism originally stems from constructionism, but has also been used by those who subscribe to interpretivism. The basic premise of this theoretical framework is that meaning is shared between people within a social grouping, via the use of symbols that are used within social interactions.

George Herbert Mead was the instigator of this philosophical perspective, although he did not label his thinking as symbolic interactionism at the time. Mead wrote scholarly papers from his work, but did not publish this work in a language that was accessible to a more general audience. Posthumously, his students gathered lecture materials and memories of conversations, and wrote of his work (Lauer & Handel, 1977).

Blumer was one author who wrote extensively about Mead's work. Blumer stated three basic interactionist assumptions:

> 'that human beings act toward things on the basis of meanings that these things have for them';
> 'that the meaning of such things is derived from, and arises out of the social interaction that one has with one's fellows'
> 'that these meanings are handled in, and modified through an interpretive process used by the person in dealing with the things he encounters' (Crotty 1998, p. 72).

Mead (1934) used a simple example of an exchange between two dogs to illustrate this basic theoretical perspective:

> The act of each dog becomes the stimulus to the other dog for his response. There is then a relationship between these two: and as the act is responded to by the other dog, it, in turn, undergoes change. The very fact that the dog is ready to attack another becomes a stimulus to the other dog to change his own position or his own attitude. He has no sooner done this than the change of attitude in the second dog in turn causes the first dog to change his attitude. We have here a conversation of gestures (p. 42-43)

The gestures used by the dogs had meaning for other dogs. The exchange of meaning occurred through an interaction. Each dog interpreted the sequence of gestures and body movements, which resulted in a shared meaning, the intention to fight.

The basic premise behind this theoretical framework is that symbols are used by people (or animals) within a social group, and the symbols have shared meaning. People outside of the

group may or may not understand the meaning. One example is language. Each nationality uses a language and some subgroups within a culture may use a dialect of that language. The symbols (vocabulary and syntactic structures) are understood by members of the group. In order to have an interaction with a member of that group, an understanding of the language is required.

Research using this framework, therefore, is not to determine which set of symbols, or which definition of a particular concept is 'correct', but to understand the symbols or language used by members of a group, and discover from the members of the group the meaning that has been attributed to the symbol set, by the members. It is not the role of the researcher, within this framework, to determine the meaning of the symbols, but simply to understand the meanings that have been attached by the members of the group.

The application of symbolic interactionism to this work allows the case studies, which include multiple perspectives, to be analysed with the aim of understanding the meaning the members of each group have given to the concepts within the ADR domain. This will provide insight into whether the decision-makers within the ADR domain have similar or different understandings of these concepts. Triangulation of the data will assist in revealing these similarities and differences. This theoretical perspective is non-critical, and so does not attempt to evaluate the appropriateness of these understandings, but seeks to understand them. We are interested in understanding the impact, if any, of these differences and similarities on the prevention, detection and management of ADRs, and incorporating this understanding when considering the requirements of ADR decision support.

3.4. Methodology – Grounded theory

The grounded theory methodology draws on the symbolic interactionist theoretical perspective (Ezzy, 2002). This section will provide an overview of grounded theory and explain how it will be used within this work, and discuss the rationale for using this approach to assist in the requirements analysis phase of systems design.

Grounded theory is a qualitative research methodology. Strauss and Corbin (1998) define qualitative research, as:

> …any type of research that produces findings not arrived at by statistical procedures or other means of quantification. It can refer to research about persons' lives, lived experiences, behaviours, emotions and feelings as well as about organisational functioning, social movements, cultural phenomena, and interactions between nations (p. 11).

Grounded theory is one of many methodologies used within the qualitative paradigm.

Grounded theory, developed by two sociologists, Glaser and Strauss in the 1960s, is a methodology that assists in the development of theory, and grounding that theory in data (Strauss & Corbin, 1998). Ezzy (2002) describes grounded theory as a methodology that "explicitly rejects the logico-deductive method of theory building and verification" (p. 7). Ezzy (2002) continues to explain the logico-deductive method as one where theories are conceptualised and then tested with data. The concept behind the grounded theory approach is that the data gathering should not be influenced by pre-existing theory, but the theory should be derived from the data.

A primary aim of this work is to go back to the beginning of the information systems design life-cycle, or even to a pre-systems design phase of understanding more about the decision-making domain, prior to even considering the requirements of the end-users of a decision support system.

The issue that was highlighted by the single case study documented in the background studies (O'Brien & Yearwood, 2002) is that even though information may exist about the potential risks of drugs, and even though this information may be available to the prescriber at the time of decision-making, and the medical practitioner at the time of diagnosis, ADRs continue to occur. Part of the problem is known to be caused by an inability to predict who is likely to experience an ADR to a particular drug. Based on this initial case study, the preliminary background studies, and previous literature, it appears that the decision-making environment surrounding the incidence of ADRs is more complex than a prescribing decision-making process, and that without understanding the interrelationships between the key actors in this decision-making

environment, decision support technology will continue to meet the perceived needs of the decision-makers, but not necessarily meet the actual needs.

In order to explore this decision-making environment, case studies of ADRs were collected including the consumer, the medical and the expert views. A grounded theory approach used to determine the factors within the decision-making environment that have an impact on the prevention and early detection of ADRs, and were seen as important from the participant's perspective rather than the researcher's perspective, is consistent with the symbolic interactionist theoretical perspective.

When collecting case studies, the definition of the ADR was provided by the person answering the advertisement. There were no entry criteria that defined the features of an ADR.

The interview (as described in the methods section below) was semi-structured in nature. Some initial questions were asked to place some boundaries around the scope of the data that were collected, however the interview moved to the aspects of the ADR experience that were viewed as important by the participant. A grounded theory approach towards the analysis of the data, has allowed the individual participant's understandings, expectations, decisions, reasoning behind their decisions, and interactions to be explored, and then integrated with current theory, or to develop emerging theory based on the data.

Grounded theory as described by Strauss and Corbin (1998), requires the detailed consideration of the data and analysis, to assist in thinking as laterally as possible about the possible meanings of each segment. This process has the goal of attempting to put aside the researcher's immediate interpretation, and determine the understanding of the participant, by going back to the participant and questioning further. They acknowledge and see as a healthy approach, that individual researchers will use the components of the methodology and modify and develop the methodology to meet individual circumstances.

Although the purpose of this research was to conduct an exploratory study and derive new concepts and theory from grounded data, the focus of the study was a specific application, one of developing decision support to assist in reducing the impact of ADRs. A modified form of

grounded theory described by Miles and Huberman (1994) was therefore chosen, that allows the analysis of the data to begin with an initial focus, rather than being completely open, as in the purest form of grounded theory. Miles and Huberman state that their preferred method of generating codes (the first stage in analysis), is to begin with a 'start list' of codes which came from prior fieldwork, research questions, hypotheses and the literature. The 'start list' came from the preliminary work described in O'Brien and Yearwood (2002) and O'Brien (2001), the literature and the research questions. This list evolved as cases were analysed, allowing the data to expand and develop the code set. The codes were then clustered and finally linked to form emerging theory.

Miles and Huberman (1994) declare themselves to be realists, in the positivist's school of thought. The aim of their approach is to be as objective as possible. Aspects, therefore, of their approach have been useful for this work, such as the idea of a 'start list' of codes, however some of their analysis techniques that are more focused on finding an objective reality have been less useful.

Strauss and Corbin (1998) describe three stages of theory development: description, conceptual ordering and theorizing:

> In brief, *describing* is depicting, telling a story, and sometimes a very graphic and detailed one, without stepping back to interpret events or explain why certain events occurred and not others. *Conceptual ordering* is classifying events and objects along various explicitly stated dimensions without necessarily relating the classifications to each other to form an overarching explanatory scheme. *Theorizing* is the act of **constructing** (we emphasize this verb as well) from data an explanatory scheme that systematically integrates various concepts through statements of relationship. A theory does more than provide understanding or paint a vivid picture, it enables users to explain and predict events, thereby providing guides to action (p. 25).

The analysis of the interview data began by generating codes, the codes were developed into a hierarchy or to use Strauss and Corbin's terminology (above), conceptual ordering, which resulted in themes. Some of the themes were combined with each other, or with pre-existing knowledge from the literature to form emerging theory.

The epistemology of social constructionism, with a theoretical framework of symbolic interactionism provides a lens when using a grounded theory form of analysis. The data were collected in the form of a series of case studies, and these case studies were analysed using three different methods of case study analysis. Section 3.5 describes these methods, and how they were applied to this research.

3.4.1. RATIONALE FOR THE USE OF GROUNDED THEORY ANALYSIS OF CASE STUDIES WITHIN THE ADR DECISION DOMAIN

Grounded theory has been used to analyse case study data to inform the requirements analysis phase of ADR decision support systems design.

Hughes and Wood-Harper (1999) used this form of analysis to understand business needs of two organisations. Gathering accurate requirements is important within the business domain to ensure the systems developed meet the needs of the business owners and the cost of the systems design is proportional to the financial benefits to the organisation.

The ADR decision domain is about preventing injury to humans. Decision support software that meet the needs of decision-makers and facilitates decision-making can assist in the prevention of injury. Decision support that is poorly designed has the potential to exacerbate the problem. Understanding the requirements, therefore, is more than providing a financial solution to assist in public health; it is about assisting in the prevention of injury to humans as the primary motivation, with an additional benefit of assisting in decreasing the financial burdens of managing these errors within the health system.

The key barrier to the use of this methodology in a business context raised by Hughes and Wood-Harper (1999) was the time taken to do the analysis, and the additional costs associated with that increased time. This issue appears to be less applicable to a decision domain that relates to public health, than it is when commercial motivators are the driving force behind systems development.

The papers reviewed in chapter two did not discuss the implication of the theoretical perspective or the epistemology underpinning their work. In the information systems (IS) literature generally, there is a discussion of the epistemology underpinning grounded theory, but this was not discussed in relation to the practical impact this has on the results of their work. It appears, therefore, that their contribution is the use of grounded theory to allow ideas about the requirements to emerge, but use a framework that suggests each core concept has a single understanding for multiple users.

As stated in the previous section, the use of a social constructionist epistemology with a symbolic interactionist theoretical perspective permits and expects that different individuals and different groups within society will construct meaning from the symbols and language used within their environments. The case studies used within the work include multiple perspectives of a single ADR, providing an opportunity to understand the different meanings each participant and group of participants have for the language used within the ADR decision domain. These perspectives can then be triangulated to provide a more complete understanding of this multi-dimensional decision domain, highlighting the areas where there is common understanding, areas where there is understanding within each group, and areas where the understanding is at the level of the individual participant.

Systems that are developed based on a single perspective, or based on an assumption that there is a single understanding of the core concepts, are likely to provide only a partial solution to a complex domain area. The use of grounded theory within this work, in conjunction with social constructionist and symbolic interactionist perspectives provides a framework for analysing the similarities and differences in perspectives between participants.

3.5. Methods – Case study analysis

This section provides an overview of the methods used within this work. It includes an overview of case study analysis (section 3.5.1), the processes of recruiting participants (section 3.5.2), challenges in recruiting participants (section 3.5.3), the processes used to collect the data (section 3.5.4) , and discussion of the analysis (section 3.5.5). Throughout this section, there is reflection of the research processes used within this work:

> …analysis is not a structured, static or rigid process. Rather, it is a free-flowing and creative one in which analysts move quickly back and forth between types of coding, using analytic techniques and procedures freely and in response to the analytic tasks before analysts (Strauss & Corbin, 1998, p. 58).

Ezzy (2002) also writes about the non-linear process of data analysis:

> For many people discovery occurs in writing as much as it does during the task of data analysis. Writing is not simply about transferring 'results' to a written page. Writing is as much about creating 'results' as it is about reporting them (p. 138).

3.5.1. OVERVIEW OF CASE STUDY ANALYSIS

The original research plan was to conduct a thematic analysis of the interview data, focusing on the views of the consumer, medical practitioner, and expert of a single instance of an ADR. The GP view of the de-identified cases in a GP forum was also to be used. Using a thematic analysis, the aim was to collect enough participants to obtain saturation. Strauss and Corbin (1998) define saturation below:

> A category is considered *saturated* when no new information seems to emerge during coding, that is, when no new properties, dimensions, conditions, actions/interactions or consequences are seen in the data (p. 136).

It became obvious, however, that although some interesting ideas evolved from the analysis of each participant group, the strength of the data came by viewing a single case. This provided insight that could not be seen by combining and grouping the data. Once the data had been combined into single cases, it became clear that the 15 cases collected, provided significant insight into this research problem. This was supported by Miles and Huberman's (1994) description of qualitative research that uses case study methods:

> With high complexity, a study with more than 15 cases or so can become unwieldy. There are too many data to scan visually and too many permutations to account for…Still we've

> seen multiple case studies in the 20s and 30s. The price is usually thinner data. And at some point you say Why not do a survey? (p. 30)

> We are generalising from one case to the next on the basis of a match to the underlying theory, not to a larger universe. The choice of cases is usually made on conceptual grounds, not on representative grounds…. If you look at the cells of the sampling frame, each is essentially unique (p. 29)

For the purposes of this research, a case has been given the following boundaries. A single case may comprise of two or more of the following perspectives of a single incident of a suspected ADR: a consumer, one or more medical practitioner and two experts.

Case studies can be analysed using a variety of methods. Three methods have been used, an individual case level (a single incident of an ADR from the consumer medical practitioner and expert perspective), an analysis of the data in participant groups (consumers, medical practitioners, and experts), and an analysis that views the case studies and groups of data together.

Rather than using a single method of analysis, three levels of analysis have been used to extract the richness that the case studies provided and each level provides insight into a different set of research questions. The research questions that focus on the interaction, or differing opinions of participants within a single case study, have been addressed through the individual case study analysis. Patterns between case studies developed into emerging themes or theory when these have been viewed when combining the case studies. The questions that pertain specifically to a group of participants (consumers, medical practitioners, or experts), have been addressed in the analysis at the group level.

The table below (Table 3-1) lists the research questions in column one, and in column two lists the method of analysis that was used to address each question. Some questions were addressed using only one method, others were informed using several methods.

3.5.2. RECRUITING PARTICIPANTS

Four groups of people were requested to participate in this study, consumers who believe they may have experienced an ADR, the medical practitioner or clinicians for each of these consumers, ADR experts and a group of GPs to participate in a GP forum. The aim was to collect four views of the one incident of a suspected ADR to form cases. Sections 3.5.2.1 to 3.5.2.4 describe how each group of participants were recruited.

Research questions	Method of analysis
1) Who are the decision-makers in the ADR domain?	Group level
2) What decisions are made by each decision-maker?	Group level
3) What do decision-makers understand by the term ADR?	Group level
4) DO ALL DECISION-MAKERS AGREE ON A DEFINITION OF AN ADR?	Between group
5) How are ADR decisions made?	Group level, case level and combined analysis
6) What problems occur when making ADR decisions?	Group level and case level analysis
7) What resources are used by decision-makers: information and knowledge sources and content?	Group analysis
8) How do decision-makers contribute to the creation of new knowledge at an individual, national and international level?	Group and combined level analysis
9) How do ADRs affect people and how does this impact on decision-making?	Group level and case level analysis

Table 3-1 Method of analysis used to address each research question

3.5.2.1. Group 1: Consumers who have experienced a suspected ADR.

Consumers who believed they may have experienced an ADR within the past 12 to 18 months either answered an advertisement that was placed in a local Ballarat newspaper, or one placed to staff and students at the University of Ballarat, via a research newsletter and via a university wide e-mail. Twenty consumers responded, 15 met the selection criteria and were interested in participating in the study. The characteristics of each of the participants has been discussed in section 4.2.2.

These criteria state that the consumer:

- is over 18 years old;
- suspects s/he has experienced a moderate to severe ADR within the past six to 12 months;

- has no disability that affects cognition or language;
- does not have a psychiatric history that may interfere in their ability to perceive and accurately report their experience and;
- is not taking recreational drugs.

The rationale for these criteria was to:

- ensure participants have the ability to report their experience of an ADR;
- ensure participants are old enough to provide consent to access their medical records;
- screen for psychiatric disorders as some psychiatric disorder may affect a person's ability to perceive and report accurately their experience of an ADR;
- screen for recreational drug usage as recreational drugs are likely to compound the problem and are out of scope of the study.

Each consumer responded by telephone or e-mail. Each potential participant was provided with an overview of the project via the telephone, was posted a plain language statement written for consumers (Appendix B), and a copy of the consent form (Appendix C), prior to the interview.

3.5.2.2. Group 2: The clinicians who treated the consumer participants

The consumer participants provided details of each medical practitioner and clinic attended throughout the experience of a suspected ADR. These medical practitioners may have been from any health service within the study region. A decision was made to limit recruitment of hospital medical practitioners to the study region, as ethics clearance had been obtained by the hospitals involved. Two medical practitioners from private practice who lived outside of the region were requested to participate in the study.

The medical practitioners named by the consumers were approached individually to request participation in the study. An information package was sent to each medical practitioner. The information package included an introductory letter (Appendix D), a plain language statement that had been written specifically for medical staff (Appendix F), a copy of the consent form signed by the consumer (Appendix C), and a blank consent form for the medical practitioners to sign if they decided to participate in the study (Appendix F). The medical practitioners were

offered a payment of one hundred dollars per hour to compensate them for time they put into the study.

3.5.2.3. Group 3: Members of ADRAC who are experts in the area of ADRs

The chief medical officer for the adverse drug reaction unit at the Therapeutics Goods Administration (TGA) was approached for assistance with this study. Two members of ADRAC volunteered to participate in the study in the role of ADR experts. One member was unable to continue with the study, and so a third member volunteered. Of the three experts, two have medical training, and one has a science background. Throughout the data collection phase of the study, one of the experts was unable to continue with the role and so another volunteer was requested who continued with the role of expert. This third expert had a medical background.

3.5.2.4. Group 4: General Practitioners to participate in a forum

GPs for the planned GP forums were recruited through a Division of General Practitioners. Leading up to the request, several articles were written for the division newsletter over a period of three months, to alert medical practitioners to the existence of the project.

The forums were developed in collaboration with the GP division and a TGA medical officer and were packaged in the form of ADR training. The Royal College of General Practitioners approved the forums as a professional development activity, which allowed the medical practitioners to gain professional development points for attendance. The planned forums included a meal, and the GPs were also offered a financial incentive to attend.

The aims of the GP forums included the following:

- to inform the GPs of the research being conducted at the University of Ballarat;
- to present of a number of the case studies collected in this work for the GPs to discuss in small groups. The case studies were to be presented by the principal investigator, and the initial learning was to be from discussion with each other about the likelihood the symptoms were caused by the suspected drug and the processes surrounding this decision-making;
- the cases were to be presented a single view at a time, and the GPs would have the opportunity to make a diagnosis initially based on one view only of the case study. This was

to be followed by the presentation of the second view and then finally the third view of the data collected. The aim was to determine if the additional information available from each view made a difference to diagnosis, and to understand more about the impact it had;

- to review of the case studies with a medical officer from ADRAC, who would:
    - answer GP questions about the cases;
    - highlight key factors within the case studies;
    - provide general information about methods of preventing and detecting adverse drug reactions in their patients;
    - provide general information about ADRAC voluntary adverse drug reaction reporting processes.

The responses from the GPs throughout the forum were to be recorded, de-identified, and with GP consent, used as the forth phase of data collection in the work of this thesis.

The forums were advertised via a 'fax out' process used regularly by the BDDGP. This process was conducted twice. GPs who had not previously been involved in the study as medical practitioners were requested to participate in the study. Three GPs from the division volunteered to participate. Following a discussion with the BDDGPs, the ADRAC medical officer and the research team, it was decided to cancel the forums due to insufficient numbers.

3.5.3. CHALLENGES IN THE RECRUITMENT PROCESS

3.5.3.1. Challenges in recruiting consumers

Significant thought was put into an effective method of recruiting ADR cases. As the goal was to collect four views of a single suspected ADR, the choices ranged from attempting to capture ADRs as they occurred to requesting the consumers to recall their ADRs retrospectively. It was decided that it was not practical to observe consumers in a clinical environment and collect cases of ADRs as the incidence of ADRs is sparse compared with the number of cases seen within a practice. It was decided, therefore to collect retrospective case studies.

There were a number of options regarding who to approach to gather the case studies such as beginning with the consumer and tracing back to the medical practitioners, beginning with the medical practitioners and tracing back to the consumers or beginning with hospital records and

tracing back to both consumers and medical practitioners. It was decided to begin by recruiting consumers and then trace back to find the medical view for two main reasons:

- In order to collect the data, consumer consent was required. Beginning with a self-selection process ensured consumer consent was obtained, and assisted in maintaining privacy.

- Medical staff could have been approached and asked to put forward cases of consumers who may have experienced ADRs. Issues raised by medical staff to this proposal included the following:

    - Some consumers may not be aware they have experienced an ADR.
    - The medical staff and/or hospital would need to contact each of these people to see if they are prepared to participate in the study maintaining strict confidentiality, until such time as the consumer signs a consent form to release their details to the research team, which is time consuming for medical staff who are already time constrained.
    - Medical litigation may result from drawing attention to suspected ADRs, especially in light of the fact that the cases at that stage are suspected rather than confirmed, and in the majority of cases the probability that a particular drug is associated with a symptom or set of symptoms is less than 100%.

Thought was also put into the specific type of ADRs to target. An initial suggestion was to collect a homogeneous group of suspected ADRs, such as ADRs from a particular drug, or reactions of a particular type such as allergic reactions. Given the complexity in collecting case studies described in section 3.5.4, it was decided that choosing a subset of ADRs would have added to the complexity of data collection, and decreased the usefulness of the results. If a common ADR had been chosen, one which was well known by the medical and perhaps the consumer community, decision-making is likely to have been different compared with an ADR that is less well known. If a rare ADR had been chosen, the numbers would have been sparse, and collecting a large enough sample, would have been more complex. If an ADR diagnosis had

been one of the selection criteria, the case studies where there is no clear diagnosis would have been missed.

As a result of the complexities above, it was decided to begin with consumers who were self-selected, and allow the spread of ADR types to be determined by who volunteered, rather than choose not to study this domain due to the difficulties in data collection.

The self-selection process may have resulted in attracting a subgroup of consumers who met the criteria. The consumer group appeared to be particularly analytical, as several of the participants maintained detailed diaries over a number of years, and the majority used logical processing to determine the likelihood that the medication taken caused the suspected reaction.

It is also possible that the consumers volunteered for the study because they were particularly concerned, angry or frustrated by their suspected reaction. As can be seen from section 4.2.2 referring to participant characteristics, the group did have a significant level of concern, with 67% displaying a high level of concern as observed by the principal researcher. It is not known if this level of concern is due to self-selection, or whether it is representative of consumers who have experienced a suspected reaction to a medication.

3.5.3.2. Challenges in recruiting medical practitioners

Usually, when requesting participation in a research study, a selected sample is chosen as a subgroup from a wider population. In this case, participation was requested from particular individuals.

It may have been possible to collect more case studies which included the medical view, if a process had been followed of recruiting the consumer participants then contacting the medical practitioners to request participation prior to interviewing the consumers. In-depth interviews would only have been conducted, then, in cases where the medical practitioner had agreed to participate. This method, however, may have excluded case studies that were of particular interest to the study, and excluded consumers who particularly wanted to participate.

By using the approach taken there are two distinct groups of case studies, those, which include the consumer, medical and expert views, and those, which include only the consumer and expert views. This provided insight into the value of consumer only views of ADRs, which would not have been as clear if all case studies had included a medical view.

3.5.3.3. Challenges in recruiting ADRAC experts

One potential difficulty may have been location of the experts as they are based in Canberra, Australia. Due to effective e-mail and telephone contact and face-to-face meetings throughout the research process, the distance has not been an issue.

3.5.3.4. Challenges in recruiting GPs

There were several challenges in recruiting GPs. The GPs have stated that they have high work demands, and are frequently requested to participate in research projects, and professional development, and so they need to prioritise according to what they perceive to be their highest needs. Many of the GPs within the division had already participated in ADR research: eight GPs from the division participated in the forums for the preliminary background studies, which were four forum sessions of one hour each; four GPs participated in the larger research project as medical practitioners; and three more GPs were interested in attending the GP forums. Projects in the area of ADRs have also been occurring within the same region and so it is possible that the GPs who do have a specific interest in ADRs had already contributed.

The GPs involved in the forums conducted in the preliminary background studies (O'Brien & Yearwood, 2002) stated that although they consider ADRs a problem which need to be addressed, their perception is that ADRs occur infrequently within the GP context and so are a lesser priority for training purposes than issues that occur more frequently.

3.5.4. DATA COLLECTION

An overview of the data collection process is presented in Figure 3-1.

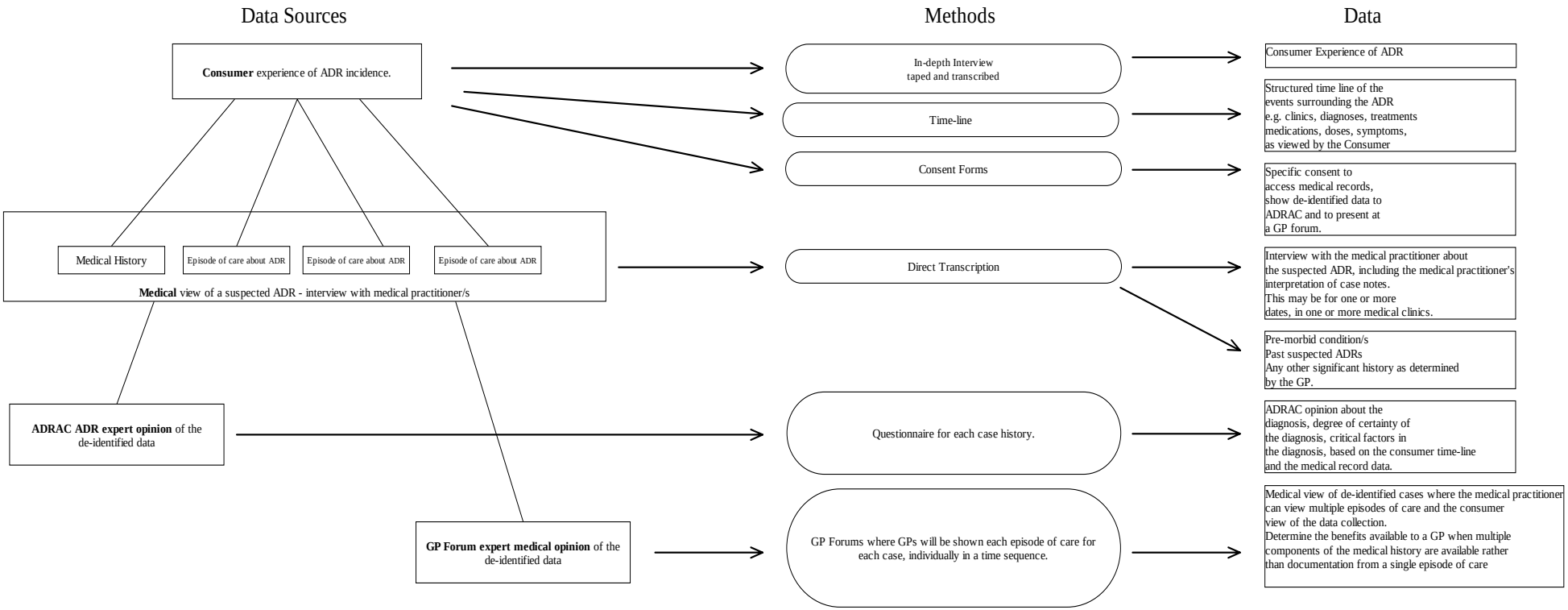

Figure 3-1 Methods of intended data collection

3.5.4.1. Choice of evidence

According to Yin (2003), one attribute of a 'good' case study has, multiple forms of evidence available to build the case, and as much evidence as possible, within the case boundaries has been collected. (Yin, 2003)

Considerable thought was put into methods of collecting evidence or data. The broad goal was to collect data about the suspected ADR from the consumer perspective. Maintaining consistency with the symbolic interactionist theoretical framework, the aim was for the consumers to talk about the aspects of the event that were important from the consumer perspective, and so an in-depth interview was selected. As a secondary aim was to collect some specific factors about the case such as relevant dates and medications, the in-depth interviews were semi-structured in nature to allow specific information to be collected, as well as allowing the consumer to direct the interview in the direction important to him or her. The time-line of events (Appendix I), a more structured form of data collection, had the aim of assisting with recall, but also collecting the medical 'facts' to assist in locating the relevant components of the medical history, and to assist the experts in making a medical diagnosis.

The next type of evidence to be considered was the medical record. The initial goal was to access the medical record directly. There were some issues with this approach. These include consumer privacy, in particular surrounding notes in the case history that were not relevant to the suspected ADR, and also reliable interpretation of the notes. As the researcher collecting the data was not medically trained (although a professional in allied health), it was decided that asking the medical practitioner to interpret the notes, would be a more reliable method of accessing the medical records.

It was decided, therefore, for the medical records to be accessed via an in-depth semi-structured interview with the medical practitioner. The semi-structured interview type was again used, to allow the medical practitioner to direct the interview to information considered relevant and important to the medical practitioner. Again, because the secondary aim was to collect the medical 'facts' of the case, specific questions were asked. A secondary benefit of the semi-structured interviews was the ability to follow up on emerging themes from the consumer data collection, and from previous interviews with medical practitioners. In some cases, the medical

practitioner, having interpreted the case notes, photocopied relevant documentation such as lab reports for the study.

All of the data collected were imported into and stored in the NVivo software program described in section 3.5.5. An inventory of the data included in that database can be found in Appendix J.

The fourth form of data collection was the opinion of ADR experts. A questionnaire with specific questions and open-ended questions was developed to access information from the ADR experts. There were a number of reasons for this approach. Two experts were asked to participate in each of the 15 case studies, and so the time required of the experts was significantly higher than the other participants. In-depth interviews about each case appeared to be a method that would be too time-consuming for this group of participants. Open-ended questions were included to allow the experts to comment on issues they felt were relevant that had not been asked by the previous questions. The primary limitation to this method was the extraction of the reasoning behind the expert's opinion. In some cases the expert provided an explanation, and at other times, further explanation was required. The experts were then prepared to answer questions via e-mail to clarify any issues. The e-mails with the experts have either been stored as memos in NVivo, or have been appended to the end of the questionnaire file.

Another data type collected from the experts was a trail of what they considered to be the key data used in decision-making. Each expert was asked to use a highlighter pen to select the data used when making a differential diagnosis. As previously stated, the case studies were compiled attempting to include the most relevant components of the data. These highlighted pieces of text, collected from the experts, were used to check that the data considered relevant to differential diagnosis, by the experts, was included in the case studies.

3.5.4.2. Methods of data collection

The data were gathered and analysed one group at a time. The initial set of data, the consumer data, was collected, de-identified, verified and analysed, prior to collecting the second group of data. The next group of data to be collected was the medical practitioner data, which again, was

collected, de-identified, verified, and partially analysed prior to sending the de-identified case studies to the experts for an expert opinion. There was no overlap between collecting the consumer data and the medical data, however, the majority of the medical data were collected and sent to the experts. In two cases, it was following the expert data collection that some more medical data were collected, and then these two cases were sent to the experts for an opinion at a later date.

It was a conscious decision to collect the consumer data prior to collecting the medical practitioner data, for two key reasons. The first reason was to allow time to sit with and identify with the consumer group in order to understand their unique issues prior to collecting medical data, which may contradict, or provide information that altered our understanding of what was being said by the consumer group. The second reason was to allow time for themes to emerge from the consumer group so these themes could be included in the interviews with the medical practitioners. An example was the issue of consumer access to ADR information. A theme that emerged was that the consumers, as a group, wanted more information about potential ADRs prior to commencing a drug, but had experienced difficulty accessing that information from the medical practitioner.

The case studies collected would have been different if the interviews had been gathered from the medical view initially. By beginning with the consumer view, some case studies were collected where the consumer suspected an ADR, however the medical practitioner and/or the experts disagreed that the symptoms were likely to have been related to the drug. This subset of case studies provides insight into the decision-making processes surrounding ADRs, when there is a difference in understanding of the series of events between decision-makers. If the case studies had all the participants in agreement about the ADRs prior to data collection, the information relating to the processes surrounding differential diagnosis may have been less detailed.

If the data collection had commenced with the medical view, it would have been possible to determine if the consumer was prepared to participate in the study prior to the initial data collection, and therefore there may have been a larger percentage of case studies obtained that included the consumer, medical practitioner and expert view, whereas with this design, only 66%

of cases include all three views. Also, all of the cases would have been local to the study region, and presumably if the medical practitioners were prepared to participate in the study initially, each case would have included the medical practitioner perspective. By collecting data beginning with the consumer, as stated previously, the consumers may have been a particular subgroup of consumers who have experienced a suspected ADR. The same can be said for the medical practitioners, there may have been a particular subgroup of medical practitioners who volunteered for the study providing a limited view of how medical practitioners in general approach this problem. As a consequence, whichever way the data might have been collected, there would have been benefits and limitations.

3.5.4.3. Group 1: Data collection from consumers.

Each consumer participant was asked to do the following: participate in a single in-depth semi-structured interview with the principal investigator, assist in completing a time line of events surrounding the suspected ADR and sign a consent form for participation in the study, and to provide permission for the medical practitioners to be contacted regarding their participation in the study.

The interview took place in a private office at the University of Ballarat or in the participant's home. The participant chose the location of the interview. The interviews were tape-recorded.

In-depth semi-structured consumer interviews

The interviewer and the participant sat at a table, with the tape recorder between them, but to one side. A micro-tape recorder was used with an external stand-alone microphone to ensure clarity of the recording. The tape recorder was small and unobtrusive however the external microphone was more obtrusive. Some participants appeared to be very aware and self-conscious of the microphone. One participant spoke directly into the microphone, and asked several times if she was 'doing it right'. A less obtrusive microphone may have assisted in providing a more relaxed atmosphere.

The interviewer disclosed the following during the introduction to the study:

- The Therapeutics Goods Administration and a division of GPs were involved in and supporting the study.

- The medical practitioners would be asked to be interviewed about the medical view of the suspected ADR.
- The interviewer is not medically trained, but interested in the broader view of the ADR experience than purely the medical acts of the case.

The effect of this disclosure appeared to be three fold. Firstly, the consumers being aware that the interviewer was not medically trained, named specific drugs, but then explained their understanding of the reason they were taking the drug and their medical condition. One consumer said that she felt comfortable knowing that the interviewer was an impartial observer rather than a medical practitioner.

The second effect appeared to be that the study took on credibility in the eyes of the consumer, knowing that it was supported by the medical community, and that they were interested in finding out more about the consumer's experience.

The third effect appeared to be that some consumers were slightly guarded in their discussion about their relationship with their medical practitioner. When asked a question about whether there was anything they would have liked their medical practitioner to have done differently, several appeared quite defensive, and then explained how supportive their medical practitioner had been, even though prior to the question, they had been quite critical of some aspects of their care. One consumer was very open about the relationship with his medical practitioner, but then checked with the interviewer that his medical practitioner would not have access to the transcript.

A goal of a semi-structured interview is to have some specific questions to ask each participant, but also to have the freedom within the interview to explore issues raised by the participant that were not previously considered by the interviewer.

The qualitative research approach also encourages the researcher to collect some data, do some analysis, and on the basis of the analysis, modify the questions for the next group of participants to explore newly raised issues.

An initial list of questions were used, that came from the preliminary background studies and the research questions. Refer to Appendix H for the list of questions asked.

The questions were not asked in any particular order. Sometimes the consumer answered a question without it specifically being asked. The interviewer intentionally attempted to create a sense of a conversation about what happened, rather than the feeling of an interview, to encourage the participants to 'chat'. This allowed issues important to the consumer to be raised, even if, on the surface, they did not appear to be directly relevant to the study. Some of those issues have become important components of the study, such as in one case, an elderly man was speaking about his progressive disability, and how quickly he had lost mobility. He progressed to speaking about the challenges he and his wife were experiencing as they both have a disability. This then provided a context for the impact of the suspected ADR. Without the life context, the impact on the consumer would have been understood differently. This outcome of the interviews is not something that was anticipated by the interviewer prior to conducting the interviews.

Questions asked and issues that were explored in later interviews due to the responses from the earlier interviews can also be found in Appendix I.

The interviews ranged in time from half an hour, to two hours depending on the level of complexity of the case.

Time-line of events

A second strategy used to assist with memory recall, was to work with the participants to complete a timeline of events (Appendix I). The aim of this timeline was to ensure that the sequence of events surrounding the suspected ADR was clearly recorded, with dates when available, so that the medical practitioners would be able to locate the episode of care within the consumer case history. This was a method of ensuring all of the medical 'facts' of the case were pieced together, including dates, symptoms, medical practitioners, drugs and dosages.

In some cases, the interviewer had enough information from the interview to complete the time-line of events and so did not ask the consumer to do what would have been a repeated activity.

In other cases, the act of filling in the time-line with the consumer prompted the consumer's memory, and additional information was raised. In two of the cases, the details of the case were so complex, that the interviewer decided to attempt to do the time-line independently based on the information obtained from the interview, and then sent the time-line back to the consumer with the interview for verification. In one case the consumer then contacted the interviewer and asked to discuss the time-line one more time. Modifications to the time-line were made during the second interview. Although the consumer continued to discuss the case in the second visit, the interview was not tape-recorded, as the interviewer had not anticipated this additional discussion and did not have the tape recording equipment with her.

Each participant was asked to complete a consent form either prior to or during the interview, with the medical practitioner's names and the address of each clinic. Most participants came to the interview with the consent form completed.

In some of the cases, the consumers provided specific dates of the consultations. In these cases where there was also a medical view for the case, the dates provided by the consumers were accurate. In the cases where the consumer was only able to provide an approximate date, it directed the medical practitioner to a section of the medical history, and then the medical practitioner was able to locate the specific consultation referred to by the consumer. There were no cases where the consumer indicated a date or approximate date, and the medical practitioner was unable to locate the specific consultation being referred to by the consumer, within the consumer's health record.

Transcribing and de-identifying consumer interviews

Approximately 80% of the tapes were transcribed by an external transcriber, who signed a confidentiality agreement. The remainder were transcribed by the research team. The transcriptions were then validated by listening to each tape and checking the transcription for errors. The tape recordings were de-identified in the following ways:

- The transcriptions were labelled with codes. For example, consumers were labelled in the following way C01, C02, C03.

- For each consumer, there may have been a number of consultations. Each interview with a medical practitioner was identified as belonging to a particular consumer, identified by the clinic type (hospital, GP), and according to their sequence. For example, if consumer C01 had indicated she attended three clinics GP1, GP2, H3. The code for the second clinic would be C01GP2. All of the data collected that related to the consumer 01, would begin with C01.
- All medical personnel's names were removed and replaced with a code. For example, Dr x may be replaced with D1. These codes were then replaced with pseudonyms in the case studies and analysis of the case studies sections.
- All consumer names were removed and replaced with a code. These codes were then replaced with pseudonyms in the case studies and analysis of the case studies sections.
- All references to relatives were removed and replaced with a code. For example, a wife's name may be replaced with W.
- In some cases the description given by the participant about his/her work environment was detailed enough to identify the participant. In these cases wording was changed from specific details to general, and then checked with the consumer to ensure meaning was not changed.
- Dates were changed, maintaining original spacing between the dates.
- All drug names were checked against a drug dictionary to ensure the drug specified by the consumer was spelt correctly. Misspelling can result in a misidentification of the drug, as different drugs exist with similar spelling. In some cases, the consumer spelt the drug name for the principal investigator, but when the drug was checked the spelling was incorrect. Drug names were then checked first by the consumers when the transcriptions were verified, and then by the experts when the de-identified cases were being reviewed by the experts.

Verification of the transcripts by the consumer participants

Transcripts and completed time-line of events were sent back to the consumers for verification in all cases except one. One participant was an elderly lady who had expressed at the time of the interview that she had been very upset by the suspected ADR, and that she wanted to hand the information over to the researcher as a way of 'letting go'. There was a nine-month gap between the interview and when the transcript was ready for verification due to an interruption to the

research process. It was decided not to send the transcript back to this consumer as it was felt that it may arouse the feelings surrounding the suspected ADR again.

Thirteen of the 14 participants acknowledged that they had received the transcript by either posting or e-mailing it back, or by phone call and either made some changes or confirmed that it was representative of the interview. One consumer did not respond.

Two participants chose to make significant changes to their transcripts. One participant chose to re-write the interview, and one asked for a second meeting with the researcher to clarify some dates and events in the timeline of events.

3.5.4.4. Group 2: Data collection for medical practitioners

The data collection process for the medical practitioners followed a similar path to that of the consumers. Each medical practitioner who chose to be involved, participated in an in-depth semi-structured interview with the interviewer, in the medical practitioner's work place. Initially the plan was to ask the medical practitioner to fill in a time-line of events. It became obvious fairly soon within this phase, however, that the medical practitioner accessed the medical record based on the consumer time-line, and so adding to the consumer time line with information such as specific dates or dosages that the consumer may not have recorded, and compiling a combined time-line was more useful.

In-depth semi-structured medical interviews

Each medical practitioner was asked if he[4] would be prepared to have the interview tape recorded. Three of the eight medical practitioners chose not to have the interview tape recorded, the remainder agreed. The interviews where a tape was used were longer and more detailed. The interviews where the interviewer was unable to tape were briefer, as the recording of the interview was in the form of note taking, which restricted the level of detail that could be recorded and also restricted the flow of the interview. Also, the medical practitioners tended to use extensive medical terminology in the interview, and some spoke very quickly limiting what

[4] Generally when referring to participants the term "s/he" has been used to indicate gender. As each of the medical practitioners in the study are male, when referring to the medical practitioners, the term "he" will be used.

could be recorded. When the interviews were tape recorded, the interviewer could listen multiple times and check the terminology to ensure accuracy.

A list of questions was compiled based on the research questions, the background preliminary studies, the literature, and the results of the consumer interviews. Several of the medical practitioners asked to see the list of questions either prior to the interview, or prior to consenting to having the interview tape recorded. As in the consumer interviews, the tone of the interview was kept conversational to encourage issues not directly asked by the interviewer, but seen as important by the medical practitioner, to emerge.

The list of questions about the suspected ADR did not alter significantly throughout this phase of the data collection. Some questions were asked explicitly, some were answered throughout the course of the interview, some were not relevant based on the answer to the previous question, and some over the course of the interviews became less relevant.

Transcribing, de-identifying and verifying medical interviews

Each tape was transcribed, de-identified, and returned to the medical practitioner for verification, unless the medical practitioner had stated specifically that he did not want to check the transcription. All interviews that were recorded by notes were sent back for verification.

Each interview was de-identified using the same methods as described in section 3.5.4.

3.5.4.5. Group 3: Data collection for experts

Once the data from the consumers and medical practitioners had been collected and de-identified, the data were sent to the participants from ADRAC for an expert opinion. The data had been organised into cases, and so for a single case, the experts received the consumer interview, the time-line of events and, if available, the medical interview. The experts, therefore offered an opinion on all case studies, those with both the consumer and medical perspectives and those with only the consumer perspective.

The ADR experts were asked to read each interview, highlight using a highlighter pen, which pieces of information within the case study they used to make their decisions, and then fill in a

questionnaire about each case study. A copy of the questionnaire can be found in Appendix G. The experts were asked to use whatever resources they would normally use when attempting to determine if they believed a set of symptoms are associated with a medication, however they were asked not to discuss the case studies with each other.

The experts then e-mailed back a soft copy of their interviews so they could be easily imported into the analysis software, and posted back the original interviews with the highlighting. Minimal de-identification was required for these data, as the experts analysed data that had been de-identified. Each expert was allocated a code, and so the experts were identified by code rather than by name. Each expert was allocated a code, E1, E2, and E3.

3.5.5. METHODS OF ANALYSIS

The analysis of these data was performed using three methods: individual case study analysis; analysis of participant groups (consumers, medical practitioners and experts); and a combined analysis viewing all of the data together.

The analysis was conducted in a different order to that in which it is presented. The group analysis of the consumers was conducted as the consumer data was collected. This was followed by a group analysis of the medical practitioners and then experts. The individual data analysis was performed at the same time as creating the case study documents, and following the group analyses. The combined analysis occurred as the final phase of analysis.

The group analysis extracted results that could only be seen when viewing that particular group of data, such as insights provided by the consumers. Once the group analysis had been completed, themes began to emerge. The analysis of the individual case studies highlighted issues specific to that individual case study; some of which were seen in other case studies, and some which were unique to that case study. It also replicated results that had been revealed during the group analysis. The combined analysis provided themes that were only visible when viewing the themes from the group data and those emerging from the case study data together, and in some cases evolved into emerging theory.

The analysis process was not linear. One form of analysis triggered insights into other forms of analysis. Some insights at the combined analysis level emerged throughout the data collection, others became clearer when writing a set of results or a research paper, and others emerged when specifically focusing on this form of analysis.

The group analysis involved coding the data and then observing patterns and emerging themes, which are described in section 3.5.5.1. The case study analysis was performed using a less formal method, and is described in section 3.5.5.2. The combined data collection method is described in section 3.5.5.3. As stated above, the order of presentation of the results is different to the order the data were analysed, and this has been explained in the introduction of chapter four.

3.5.5.1. Group analysis

The process of coding involves attaching codes to data. In this case the data comprises the consumer and medical practitioners' interviews, the expert questionnaires, and additional documentation such as letters or notes from medical files. Miles and Huberman (1994) describe codes:

> Codes are tags or labels for assigning units of meaning to the descriptive or inferential information compiled during a study. Codes usually are attached to "chunks" [of text] of varying size – words, phrases, sentence, or whole paragraphs, connected or unconnected to a specific setting. They can take the form of a straightforward category label or a more complex one (e.g. a metaphor) (p. 56).

According to Strauss and Corbin, it is not necessary to code every interview in minute detail, but important to perform very detailed coding at the beginning of the analysis process, in order to establish the key concepts held within the data, and then to scan the remaining data for new ideas or concepts that had not been previously captured, (Strauss & Corbin, 1998). Miles and Huberman (1994) warn that it is easy to be overloaded with the enormity of the task, and the very large quantity of data that can be generated. They, therefore, suggest being selective in the process of coding, using research questions and the conceptual framework to hone in on the relevant concepts and ideas. "You may never have the time to condense and order, much less to analyse and write up, all of this material" (p. 55).

Following Miles and Huberman's (1994) recommendations, the coding was begun with a set of codes that were derived from the research questions, the preliminary background studies, and the literature.

The data analysis tool, NVivo 2.0 (QSR, 2002) was used to assist with the initial coding of the data. NVivo is a software package designed to assist with the process of coding, it does not do the coding for the analyst. Some features of NVivo that were extremely useful during the coding process were the ability to generate codes and store them electronically, attach code tags to the data, with the ability to code the same data in different ways (sometimes a phrase or paragraph can relate to more than a single concept.).

In the purest form of grounded theory, 'free nodes' are created and the codes are then grouped and clustered in the second phase of analysis to form tree structures, or hierarchies. The codes naturally developed into hierarchical structures, which were represented within NVivo as tree structures, and so allowed this process to naturally occur.

Themes emerged from these codes that relate to each of the research questions. As will be explained in detail in the results chapters (chapters four and five), the results will be presented using the research questions as the primary structure, followed by the themes at the second level.

3.5.5.2. Individual case study analysis

The individual case studies were analysed using a less formal method than the group analysis. The individual case studies were compiled from the raw data, and are presented in chapter four. Throughout the process of creating the case studies, insights into the decision-making processes within the case study emerged. At an individual case study level, all that can emerge is a concept or idea that relates to that case study. It cannot be a theme at this stage, as it has only occurred a single time. As each case study was compiled and analysed, themes between the individual case studies began to emerge. These themes could then have been re-presented in a results section looking at the between case study themes, but rather than introducing this repetition, the emerging themes at this level are re-presented in chapter five, which discusses the results in the

context of the entire set of results and comparing it with current knowledge found in the literature.

The repetition between the individual case studies indicated triangulation between the individual case studies. As the individual case study analysis revealed some concepts that had already emerged in the group analysis, the only ideas to be presented in this section are those that were unique to the individual case study analysis, and were not revealed in the other forms of analysis.

3.5.5.3. Combined methods analysis

The combined analysis primarily occurred whilst conducting the other two forms of analysis. There were themes which arose from either the group analysis, or gradually when doing the individual case study analysis, that when combined produced either more detailed themes, and in some cases emerging theory. These results were only visible when all of the data and the results of the previous forms of analysis, were combined. These are presented in section 5.5.

3.5.5.4. Triangulation

Triangulation is a term which is often used to support evidence. Patton (1987), cited in Yin (2003) describes four types of triangulation. These include triangulation:

- of data sources (data triangulation);
- among different evaluators (investigator triangulation);
- of perspectives to the same data set (theory triangulations); and,
- of methods (methodological triangulation) (pp. 98-99).

The analysis of case study data was triangulated in a number of ways. The triangulation "of data sources" (Patton, 1987 cited in Yin, 2003, p. 98), included triangulating the views of the consumer, medical practitioners and experts. In some cases, there was "convergence of evidence" (p. 100) described by Yin (2003). This term meant that when multiple sources of evidence are used, they can confirm or validate a 'fact'. The use of triangulation for this purpose fits within a positivist theoretical framework, as the goal is to find a single understanding for a concept. The data have been triangulated within these case studies using a symbolic interactionist theoretical framework. Rather than using multiple sources of evidence to confirm

a 'fact', multiple sources of evidence have been used to reveal differences in understanding between individuals within a single case study, and between the groups.

Another example of triangulation was when the individual case studies revealed themes that were repetitive. Rather than describing each of these repeating themes within the individual case study analysis, these themes were extracted and reported using the group and combined methods of analysis.

These uses of triangulation added strength to the results of these three methods of data analysis.

3.6. Ethical considerations

The University of Ballarat Human Research Ethics Committee reviewed the research proposal, and due to the complexities of the project and the sensitivity of the data, agreed to a meeting to discuss and work through ethical concerns. Following the discussion, the ethics committee requested that some additional measures be taken to ensure participant safety, and for the project to be re-submitted for consideration following these changes. The second time the project was submitted, it was approved on 27th June 2002, subject to the approval of the Ballarat Health Services and St. John of God Health Services, Combined Hospitals Ethics Committee. The research proposal was approved by the Ballarat Health Services and St. John of God Health Services, Combined Hospitals Ethics Committee on 26th August 2002.

The University of Ballarat Human Research Ethics Committee also required that the other participating bodies, put in writing that they did not need the project to be approved by their own ethics committees.

Ethics approval was obtained by all of the organizations involved in the study, as requested by the University of Ballarat Human Research Ethics Committee. Care has been taken to ensure that all of the requirements of each of the ethics committees were adhered to, and to avoid ethical issues that may impact on any of the participants.

One unanticipated ethical issue that arose was the issue of de-identification of case study material when it was presented within the thesis in individual case study format. The consumers were told by the interviewer that the contents of their transcript would not be discussed with the medical practitioner, and that the interview with the medical practitioner would not be discussed with the consumer. The consumers were aware that the information recorded within the time-line of events (containing the medical 'skeleton' of the cases) would be disclosed to the medical practitioner, to assist in the location of the particular episode of care within the consumer's medical case history. The consumer consent form included a request for the consumers to give the interviewer permission to contact the medical practitioners who were involved in the suspected ADR. Care was taken throughout the interview process to ensure information other than what was included in the time-line of events, was not disclosed to the medical practitioner. Case study analysis, however, meant that the individual interviews were situated next to each other as a component of the research analysis. The data have been carefully de-identified, including changing names, locations, and dates (but maintaining relationships between dates), and at times aspects of the interview that would identify a participant, such as comments about work environment. This issue was particularly important when studying people from a regional centre. This process has minimized the likelihood that someone outside of the case study would identify the participants. The participants themselves, however, if reading the results of this study, would potentially be able to identify themselves within the study.

Advice was sought regarding this issue, and a number of possible suggestions were raised. These included: further de-identification of the case studies; removing the individual case study analysis and using only combined case study analysis and the group analysis; an embargo; or restructuring the thesis so the case study data is in a separate volume within limited access. Each of these has been discussed below.

3.6.1.1. De-identify the case studies

The suggestion was to de-identify the case studies to the point that the individual (consumer and/or medical practitioner) who participated in the research cannot identify his/her own case. As there are only 15 case studies, using the process of elimination, the participants can reasonably work out which is their case.

The method used within this research of interviewing the medical practitioners rather than, as initially proposed, collecting the medical view from the consumer medical histories, was to ensure medical integrity of the data. The medical experts involved in the study, ensured terminology was correctly used, and explanations based on the medical data were credible. The 'skeleton' of each case study includes the medical details such as the drug names, dosages, symptoms, and temporal relationship between these factors. The decisions and interactions between the decision-makers, which form the main body of the discussion and conclusion, 'hang' off this skeleton. Each case, at this level, is unique, and therefore potentially identifiable by the consumer who participated in the interview.

Another suggested method of assisting with the de-identification process was to remove the drug names. The participants, however, would still be able to identify his or her own case by other factors within the case study. To illustrate, below is a small segment of one case study.

> Joanne, a 29-year-old woman, who works in a health profession, has a significant history of allergies, in particular an anaphylactic reaction to nuts. Joanna experienced three suspected ADRs, the most severe one a suspected photosensitivity reaction to Celebrex, which resulted in ongoing photosensitivity for at least two years.

Below is the same segment from a case study. The gender age and occupation have been changed and drug names removed:

> Ray, a 35-year-old man has a significant history of allergies, in particular an anaphylactic reaction to nuts. Ray experienced three suspected ADRs, the most severe one a suspected photosensitivity reaction to Drug A, which resulted in ongoing photosensitivity for at least two years.

Joanna would still identify her case from this segment as there is no other case study where the consumer within the set of case studies who had a history of a significant allergy to nuts and experienced a suspected photosensitivity reaction that lasted several years.

3.6.1.2. Removing individual case-study analysis

The intention was always to triangulate the multiple perspectives of the consumer, medical practitioner and expert. This was made explicit to the participants. What was not considered at the commencement of this work was how the case studies would be presented within the thesis, without allowing the consumers to have access to the medical practitioner view and vice versa.

The individual case study analysis is an integral component of this work, and accounts for more than half of the results within the thesis. Removing the individual case study analysis and analysing the case studies at a multiple case study level would severely compromise the results of the thesis.

3.6.1.3. Restructure of the thesis

A final suggestion was to re-structure the thesis into two volumes. Volume one to contain the main body of the thesis, and Volume two to contain the details of the case studies. Following examination, the second volume would not be available to the general public.

A combination of the above suggestions has been used within this work. The thesis has been structured into two volumes. The case studies have been removed from Volume one, but the analysis of the individual case studies remains. In chapter five, which presents the group analysis of the case studies, at times the participant's pseudo name has not been used, and at times the drug name has been removed. The case studies allow insight into the human side of ADRs.

There does not appear to be a totally satisfactory solution to this ethical issue. A balance, therefore, has been attempted between removing some detail to make it more difficult for a consumer who has identified his or own case, to determine the medical data that pertains to his or her case, and maintaining the human side of these cases.

3.7. Summary of research process

This study is situated in a social constructionist epistemology, with a theoretical perspective of symbolic interactionism. Case studies of consumers with suspected ADRs have been collected, which include two or more perspectives from consumer, medical practitioner and experts.

These case studies have been analysed using a grounded theory methodology, and methods have included an analysis of each participant group (consumers, medical practitioners, and experts), individual case study analysis, and analysis combining the case study and group analysis results.

Significant ethical issues were raised by two ethics committees, but were eventually worked through and resolved. Issues surrounding confidentiality of the data that emerged throughout the research process have been discussed.

Considerable thought went into the complex task of collecting data for this study, given the ethical and logistic issues that surrounded the data collection. Eventually the method of data collection included advertising for consumers who believe they may have experienced an ADR, contacting the medical practitioners and asking for their participation in the study, and passing the de-identified case studies to two ADR experts. GP forums were organised as a fourth phase of data collection, however due to a lack of numbers were cancelled.

The consumers and medical practitioners each participated in an in-depth semi-structured interview, and were asked to participate in the creation of a time-line of events. These interviews were recorded via tape recording or note taking. The tapes were transcribed, de-identified and passed to the experts. The experts highlighted on each of the transcripts the pieces of information they considered important, and filled in a questionnaire.

The data were analysed using three methods. The participant data were grouped into consumer, medical practitioner and experts and each set of data coded using the NVivo analysis software to assist with this process. The data were also analysed at an individual case study level and then finally by combining all of the data, and the results of the two previous forms of analysis.

The results of the analysis are presented in the next two chapters. Chapter four includes an overview of the data collected followed by the individual case study analysis. Chapter five includes the group analysis at the consumer, medical practitioner and expert levels, and also the results of combining the data.

CHAPTER FOUR

Results: Data Overview and Individual Case Study Analysis

4.1. Introduction

The results are presented in two chapters, chapters four and five, followed by a third chapter, chapter six, that integrates the results and discusses them in the context of past literature. The first of the results chapters (chapter four) includes an overview of the data followed by the individual case study analysis. The individual case studies have been divided into three groups, the case studies which include a consumer, medical practitioner and expert view, and there is a high likelihood that the consumer has experienced an ADR, the case studies which include again, all three groups, but where the likelihood that the consumer experienced an ADR is low, and the final group which are case studies which only include a consumer and expert view and there is a high likelihood that the consumer has experienced an ADR.

The second results chapter (chapter five) includes the group analysis which is divided into the group analysis for the consumer data, the group analysis for the medical practitioner data and the group analysis for the expert data. This is followed by the analysis when viewing all of the data.

4.2. Overview of data

This section summarises and describes the data, to provide an overview of what was collected prior to delving more deeply. This section describes the participants for each case (section 4.2.1), followed by the characteristics of each participant (section 4.2.2) and then the characteristics of the ADRs (section 4.2.3).

Case ID	Consumer	GP	Specialist	Hosp	ADRAC		
					Expert 1	Expert 2	Expert 3
C02	C02 Female	C02GP1	Declined[1]	NA[2]	C02TGA1	C02TGA2	
C04	C04 Female	Declined	NA	NA	C04TGA1	C04TGA2	
C05	C05 Female	NA	C05SP1	C05H1	C05TGA1	C05TGA2	
C06	C06 Female	NA	NA	C06H1	C06TGA1	C06TGA2	
C07	C07 Female	Declined	C07SP1	NA	C07TGA1		C07TGA3
C08	C08 Female	Declined	NA	OL[3]	C08TGA1	C08TGA2	
C09	C09 Male	C09GP1	NA	NA	C09TGA1	C09TGA2	
C10	C10 Male	Declined	NA	NA	C10TGA1	C10TGA2	
C11	C11 Female	Declined	C11SP1	NA	C11TGA1	C11TGA2	
C12	C12 Male	NA	NA	OL	C12TGA1	C12TGA2	
C13	C13 Female	C13GP1	NA	NA	C13TGA1	C13TGA2	
C14	C14 Male	Declined	NA	NA	C14TGA1	C14TGA2	
C15	C15 Female	NA	NA	OL	C15TGA1	C15TGA2	
C16	C16 Female	NA	OL	OL	C16TGA1		C16TGA3
	C16 Family[4]						
C17	C17 Male	C17GP1	NA	NA	C17TGA1	C17TGA2	

Table 4-1 Participants for each case study

1. Declined – each of these participants were sent an information package and requested to participate in the study, followed by a phone call. The participants either chose not to participate or did not respond to the request.
2. NA – not applicable. The participant did not use this service throughout the suspected ADR.
3. OL – The medical practitioners were based in a hospital outside of the regional area. These medical practitioners were not approached as ethics clearance was only for specific hospitals.
4. In this case, the consumer's husband was interviewed, as the consumer was not fully aware during the suspected reaction.

4.2.1. PARTICIPANTS FOR EACH CASE

Each case study comprises interviews from two or more perspectives. Table 4-1 lists the interviews that were obtained for each case study. In total the data collection comprises 25 in-

depth interviews (15 consumers, one family member and nine medical practitioners) and 30 questionnaires (two expert views for each case study)

Three experts are listed in Table 4-1 because of the two experts who initially volunteered for the study one was unavailable to review the final two case studies. As a consequence a third member of ADRAC offered to provide an expert opinion for the remaining two cases, and is labelled as 'Expert 3'.

The codes used to indicate the participant and participant type were described in section 3.5.4.3. To remind the reader: consumers were labelled in the following way C01, C02, C03. For each consumer, there may have been a number of consultations. Each interview with a medical practitioner was identified as belonging to a particular consumer, identified by the clinic type (hospital, GP), and according to their sequence. For example, if consumer C01 had indicated she attended three clinics GP1, GP2, H3. The code for the second clinic would be C01GP2. Each case study was reviewed by two experts, with the code TGA1, TGA2 or TGA3 to identify the expert. The interview data relating to the first expert's evaluation of C05's case therefore is C05TGA1.

4.2.2. PARTICIPANT CHARACTERISTICS

In order to understand who the participants were, their characteristics have been described in this section. Sections 4.2.2.1 to 4.2.2.3 describe the characteristics of the consumers, medical practitioners and experts respectively.

4.2.2.1. Consumer characteristics

Twenty consumers inquired about the study and 15 chose to participate. There were four consumer participants who entered the study without meeting one of the criteria. Two with diagnosed depression were entered into the study, the first because the diagnosis was not disclosed by the participant but was disclosed by the medical practitioner after the consumer interview had been completed, and the second, because it did not become apparent that the person had this disorder until partially through the in-depth interview. In two more cases, the time since the suspected reaction was greater than 18 months. It was decided to enter these four case studies into the study as they added additional information. In the cases of the depression,

in one case it was being treated, and in the other case, it did not appear to affect the participant's ability to report their experience.

The 15 consumer participants had the following characteristics:

- Age range of 29 to 76, with the following breakdown:
  - four aged 21-40, eight aged 41-60, three aged 61-80.
- ten female, five male.
- six from the University of Ballarat, nine from the community.

4.2.2.2. Medical practitioner characteristics

If, when requested to participate in the study by mail, there was no response from the medical practitioner, a follow up phone call was made to the medical practitioner's clinic. Of 16 medical practitioners approached, nine agreed to participate.

The medical practitioners had the following characteristics:

- half the medical practitioners approached were prepared to participate.
- nine male, none female.
- three medical specialists, four general practitioners, two hospital based medical practitioners.
- two hospital based, seven community based.

Information about age was not collected however the estimated age range is 30 to mid 50s.

4.2.2.3. Expert characteristics

ADRAC (Adverse drug reaction advisory committee) is the central body in Australia for collecting reports of suspected ADRs and determining the likelihood that the drugs are associated with the newly presenting symptoms. This committee is considered, within Australia, as an expert committee in ADR detection. The experts within this work are professionals working within the ADRAC Secretariat.

Two experts initially volunteered as expert participants in the study. Throughout the study, one was unable to continue with the project, so a third volunteered. The three male experts are members of ADRAC. Two of the experts are medically trained, and one is a scientist.

4.2.3. SUSPECTED ADR CHARACTERISTICS

Table 4-2 describes the characteristics of the suspected ADRs, including the reaction type classification. Reaction types were described in detail in the literature review chapter (section 2.2.4). Below is a summary of the definitions to assist in the interpretation of the information presented in Table 4-2.

Case ID	No. drugs	Drug	Symptoms Consumer view	Suspected ADR Type Expert view
C02 (Single)	Single	Tegretol[1]	Severe flu style illness	Type B
C04 (Multiple)	Multiple	tramadol hydro-chloride	Itchy/skin crawl, in absence of rash	Type A
C05 (Single)	Single	Generic sodium valproate	Grand Mal first for 18 years.	Type F
C06 (Single)	Single	Panadeine Forte	Convulsions	Type B
C07 (Multiple)	Multiple	tamoxifen	Aches in legs, and nausea	Type A
C08 (Single)	Single	Inderal	Slow heart rate and slow recovery from epidural	Type E
C09 (Single)	Single	Zyban	Bell's Palsy	Type B
C10 (Multiple)	Multiple	Efexor	Vomiting after second dose, for two weeks	Type B
C11 (Multiple)	Multiple	hydralazine	Drug induced lupus	Type B
C12 (Single)	Single	Panadeine Forte	Felt ill enough to miss work, nausea, generally feeling unwell	Type A
C13 (Multiple)	Multiple	Celebrex	Photo-sensitivity – pustule rash	Type D
C14 (Multiple)	Multiple	Vioxx	Photo-sensitivity – itchy rash	Type D
C15 (Multiple)	Multiple	Maxolon	Double vision	Type B
C16 (Multiple)	Multiple	Sabril	Induced severe seizure – similar to psychotic episode.	Type F
C17 (Single)	Single	Lipitor	Restless Legs, unwell, pain in legs and hip	Type B

Table 4-2 Characteristics of the suspected ADRs

1. Drug proprietary (trade) names have been capitalised, and generic names have not been capitalised. The consumer used either a proprietary name or generic name. The term used by the consumer has been used in the thesis.

- Type A, predictable events or reactions, pharmacological reactions or expected events or reactions, common and are accounted for by a drug's known pharmacological properties, (Kalachnik, 1999).
- Type B, unpredictable events or reactions. Also referred to as idiosyncratic or unexpected events or reactions, uncommon and independent of a drug's known pharmacological properties (Kalachnik, 1999). This group includes hypersensitive reactions. A person may have a slight reaction the first time they are in contact with the drug, but may react more severely with each subsequent contact.
- Type C, dose related and time related. Uncommon and related to the cumulative dose,
- Type D, delayed. Uncommon, usually dose related and usually becomes apparent some time after the use of the drug,
- Type E, withdrawal. Uncommon, occurs soon after the withdrawal of the drug and
- Type F, unexpected failure of therapy. Common, dose related and often caused by drug interactions. (Edwards & Aronson, 2000)

Table 4-2 lists the suspected drug name, whether the consumer was taking a single drug or multiple drugs at the time of the suspected reaction, and the suspected reaction type using the definitions above, from the expert perspective. In summary, the suspected ADRs experienced by the participants have the following characteristics:

- Type of medication – 15 prescription, no non-prescription, no complementary.
- Number of medications - seven single medication, eight multiple medications.
- three Type A, seven Type B, no Type C, two Type D, one Type E, two Type F.
- Suspected interaction between multiple drugs, one case study.

4.3. Introduction to individual case studies

As stated in the previous chapter, the process of analysis and recording results is a different process from writing the results and assisting the reader gain an understanding of the key concepts, themes and emerging theory.

The results from the individual case studies are presented first. Some of the case studies describe more than one suspected ADR, however each case study has a primary focus on one of them. The case studies have been presented in Appendix A in Volume two of this thesis[5]

Following the individual case study results, are the results from the group analysis, which are presented in chapter five. These results include any emerging themes that were viewed by analysing the consumer data, medical practitioner data and expert data separately from each other. This is followed by results that emerged when the data were combined and the results of the individual case study analysis and group analysis is combined.

A secondary element to this order of presentation of the results relates to the strength of the emerging results. The individual case studies provide insight into concepts, the group data presents emerging themes, or conceptual ordering, to use Strauss and Corbin's terminology (Strauss & Corbin, 1998). The final section that reports on results obtained by combining the data and previous results begins to describe some possible explanations emerging from the data, which becomes emerging theory.

The results have been presented using the research questions and emerging themes as a structure as illustrated in Table 4-3. Column one lists each of the research questions and the key themes that have emerged from each question. The second column indicates the primary method of analysis that was used to inform each research question. The structure is a guide only, as there were times when one method of analysis provided a small insight into a research question, an insight that was not visible when viewing the data using the primary form of analysis, and so was included, but is outside of this overriding structure. Throughout the remainder of the document, the structure of each section will include the research questions and themes that are relevant to that section.

Eight of the case studies include a consumer, one or more medical practitioners and two expert views. The remaining seven cases include only the consumer and expert view. In two of the 15

[5] As explained in detail in section 3.6, the individual case studies in volume two will not be available to the public due to the sensitive nature of the data, and the inability to protect the participants through de-identification.

case studies, both of the experts agreed that the medication was unlikely to be associated with the symptoms. In the remaining 13 cases, at least one expert agrees that there is a significant likelihood that the drug was associated with the symptoms.

Research questions and key themes	**Method of analysis**
Who are the decision-makers (defined by the participants) in the ADR domain? Multiple decision-makers.	Group level
What decisions are made by each decision-maker? Decision types. Consumers as diagnostic decision-makers. The role of the pharmacist	Group level
What do decision-makers understand by the term ADR? 'Side effect' as an attribute of a drug 'Side effect' as an expected but non-therapeutic effect of a drug 'Reaction' describing the experience of the consumer 'Allergy' as a type of reaction Terminology used when quoting a health professional	Group level
Do all decision-makers agree on a definition of an ADR? Differences in understanding	Group level
How are ADR decisions made? Differential diagnosis – Consumer Differential diagnosis – Medical practitioner Differential diagnosis – Expert Differences between GPs and specialists Medical practitioner/consumer decision-making models	Group level, case level and combined analysis.
What problems occur when making ADR decisions? Medical practitioner/consumer relationship Decision-making with partial knowledge Decisions that may contribute to an ADR Complexities in the ADR decision domain	Group level and case level analysis
What resources are used by decision-makers? List of resources used – Consumer List of resources used – Medical practitioner List of resources used – Expert	Group analysis
How do decision-makers contribute to the creation of new knowledge at an individual, national and international level? Reporting suspected ADRs to ADRAC Reasons for low levels of reporting Concerns about a lack of reporting Impact on individual decision-maker learning	Group analysis and combined analysis
How do ADRs affect people and how does this impact on decision-making? Impact on the medical practitioner/consumer relationship Perception of the severity of the suspected ADR The importance of life context Differences between expected versus unexpected symptoms	Group level and case level analysis

Table 4-3 Method of analysis used to address each research question

4.4. Case studies of suspected adverse drug reactions: high likelihood of an ADR from the consumer, medical and expert views

The following five case studies include the consumer, medical and expert perspectives of a single ADR, the case studies of Toni, Helen, Irene, Joanna and Paul. The age range is from 29 to 64 years of age. In each of these case studies, both of the experts believe there is a likely association between the suspected drug and the newly developed symptoms. The case studies have been presented in Volume two of this thesis. Below are the results of the individual case study analysis.

4.4.1. ANALYSIS OF TONI'S CASE STUDY (C02)

Toni experienced a suspected reaction to Tegretol, a reaction that resembled the symptoms of a 'flu like' virus. This case study includes the view of Toni the consumer, her general practitioner Dr Barns, and two experts. The specialist who prescribed the drugs chose not to participate in the study. In this case, all participants agree that there is a high likelihood that the symptoms are related to the drug Tegretol. The details of Toni's case study can be found in Volume two, section 1.2.1.

4.4.1.1. How are ADR decisions made?

Differential diagnosis

ADR resembles another disease

The symptoms of this uncommon ADR closely resembled a common disease, an influenza type of virus. It appears that the first time Toni went to see her GP, the most likely cause of the symptoms was diagnosed and it was not until the condition progressed in an unexpected way for the initial diagnosis that a second diagnosis was considered.

According to the experts (from the group expert data), in order to differentially diagnose between an ADR and another disease, the decision-maker/s need to be aware that a differential

diagnosis is required, and that it is important to have a drug reaction as one of the possibilities in mind at the beginning of the decision-making process. It appears that in this case, the diagnosis on the first day was a virus. It appears from this case study that differential diagnosis did not begin until the second consultation, and according to the medical practitioner the rash was what signalled the possibility of an ADR.

According to one of the experts awareness that the drug Tegretol has a potential reaction that resembles a virus, would have assisted in the diagnosis of this ADR two days earlier. The second expert said that he believes that the reaction was detected as soon as was feasibly possible given the similarity of the two conditions.

Novel versus pattern matching

In this case, there is a difference of opinion about how the diagnostic decisions surrounding the suspected ADR were made. According to Toni, Dr Barns had begun to suspect the ADR on the second visit, as he ceased the Tegretol, and was differentially diagnosing between an ADR and a virus, using temperature as a key factor. According to Toni, he stated that because Toni had a temperature, the symptoms were unlikely to have been related to an ADR. By the third presentation, the rash had developed, and Dr Barns requested liver function tests and rang the specialist, two actions to determine if the symptoms were related to an ADR.

According to Dr Barns, he recognised the ADR as an allergic reaction, based on the look of the rash. He said "it looked like a reaction", indicating he used a pattern matching style of decision-making. From this case study, therefore, it is not clear which style of decision-making was used, and perhaps there was a combination of styles.

Diagnosis based on probabilities rather than absolutes

Based on the combined accounts of Toni and Dr Barns, above, it appears that the initial diagnosis was a virus, and that the possibility of a second diagnosis required a differential diagnostic process to occur, and by the third visit, the second diagnoses became more likely than the first diagnosis, illustrating clearly that in this case, diagnosis was about weighing up possibilities with a level of probability, rather than black and white certainties.

4.4.1.2. What problems occur when making ADR decisions?

Medical practitioner/consumer relationship

Medical practitioner's awareness of the experience of the ADR

Within this case study, there are multiple instances where Toni described one experience, and Dr Barns described what he believed to be Toni's experience, with a significant discrepancy between perceptions:

- Dr Barns thought that the specialist had warned Toni of the potential problems with Tegretol, when according to Toni, he did not warn her.
- Dr Barns thought that Toni was aware that the symptoms were probably caused by an ADR, when Toni reported that she was not aware of this.
- Dr Barns believed that Toni recovered quickly, when Toni did not feel she made a full recovery for ten weeks.
- Dr Barns believes that the medical specialist reported Toni's case to ADRAC, however, he did not know for certain.

Decision-making with partial knowledge

Partial knowledge of ADRs

In this case, there were two key impacts of not providing Toni with information about suspected ADRs.

Toni reported that she specifically asked the specialist if the medication may cause problems that she should be aware of. According to Toni, the response of the specialist was for Toni to not worry about it. Dr Barns stated that he believed the specialist would have warned Toni about possible reactions, as reactions are more common with this group of drugs. One of the experts believed that if Toni had been aware that a symptom of an ADR could resemble a virus, it would have been detected and managed earlier resulting in a less severe reaction.

In the absence of reliable medical information, Toni used less reliable information sources such as discussions with family and friends. Information gathered about the "reputation" of Tegretol added to Toni's anger at not being told about potential ADRs associated with this drug,

especially when her perception was that those around her were aware of the potential dangers of this drug, but when she asked for this information, she was not given it.

Treating medical practitioner different to the prescribing medical practitioner

Toni's specialist prescribed the drug, but Toni sought treatment from her GP rather than the prescribing medical practitioner. In the preliminary background studies (O'Brien, 2001) the GPs stated that they use a 'preferred list' of drugs. This is a method they use to manage the large number of drugs available on the market. Rather than attempting to know all drugs on the market, they limit the drugs they use regularly. The drug prescribed by the specialist, may not be a drug that is one regularly used by the GP. According to Toni, Dr Barns requesting confirmation of the diagnosis from the specialist, indicating that the specialist had more familiarity with this drug than the GP.

4.4.1.3. How do ADR decision-makers contribute to new ADR knowledge? Impact on individual decision-maker learning

Lack of feedback to prescriber from consumer

In this case study, Dr Barns believed that Toni recovered quite quickly. As Toni did not feedback to Dr Barns that she took ten weeks to recover from this reaction, and Dr Barns did not follow up with Toni regarding her recovery, he did not have the opportunity to develop more of an understanding about this specific ADR.

4.4.2. ANALYSIS OF HELEN'S CASE STUDY (C06)

Helen had a mole removed in day surgery at about four o'clock in the afternoon under local anaesthetic. Following surgery she took Panadeine Forte for the pain, which resulted in her feeling nauseated, fainting and convulsing. The treating medical practitioner and experts agree that the symptoms are highly likely to be associated with the drug Panadeine Forte. The details of Helen's case study can be found in Volume two, section 1.2.2.

4.4.2.1. What problems occur when making ADR decisions?

Decision-making with partial knowledge

The impact of partial knowledge

Helen chose to take a medication not prescribed for her, a medication that resulted in a suspected ADR. The circumstances surrounding this decision, however, included a lack of information. Helen took this medication, because the pain she experienced was severe, it was the middle of the night, and she had no other medication in the house. She said that she did not expect to experience such a severe level of pain, and if she had been aware, she would have ensured she had what she needed available to her.

Helen also commented that she felt unwell when she left the surgery, but because she did not expect to feel unwell, she had her children with her and drove. She may have made a different choice if provided with information about the possible outcomes post surgery.

As the surgeon did not participate in the study, it is not known whether the medical practitioner could have predicted these symptoms and provided prior warning to Helen to assist with these issues.

Impact of no diagnosis

At the time of interview, Helen was not certain of the diagnosis. It is well known that often it is difficult to provide a clear diagnosis for a suspected ADR but it appears in this case the medical practitioner did make a diagnosis. Two impacts of not knowing about this diagnosis, have been identified from this case study. Because Helen has not been provided with a diagnosis, it is possible that she will take the medication again, even though, in the interview, the medical practitioner stated that there is a high chance that Helen would experience the same reaction again, and should avoid the drug. The second impact was that in order to understand the cause of her experience, she sought other sources of information that may be less reliable, because the people she asked did not have access to all of the information.

4.4.2.2. Decisions that may contribute to an ADR

Taking a prescription drug prescribed for another consumer

As stated previously, Helen chose to take a medication that was not prescribed for her. According to one of the experts, Helen's decision to take a prescription medication prescribed for someone else, may have contributed to the occurrence of the ADR.

4.4.3. ANALYSIS OF IRENE'S CASE STUDY (C11)

Irene has a significant history of ADRs. She spoke in detail about a suspected reaction to a drug hydralazine, which was associated with drug-induced lupus. Irene expressed concern about her failing memory combined with her history of multiple suspected reactions. In order to manage, she maintains detailed diaries of her care, which are the equivalent of her own personal medical record. Irene's specialist Dr James located the key information within his own medical history about the suspected ADR using Irene's dates to guide him. Dr James and experts agreed with Irene that there is a high likelihood that the drug was associated with the symptoms.

Irene's GP responded to the request to participate in the study by return mail. He chose not to participate in the study, however, due to a lack of time, stating that Dr James, Irene's specialist, would have the same information that he would have. The details of Irene's case study can be found in Volume two, section 1.2.3.

4.4.3.1. How ADR decisions are made?

Prescribing decisions

<u>History of ADRs</u>

According to Irene, she has a significant history to ADRs, and so provides any new medical practitioner with a list of past suspected ADRs so the medical practitioner can use this information when making decisions about drugs to prescribe. The experts stated that this history is an indicator that she is likely to be "sensitive" to future drugs. One of the experts stated, during a discussion, that if a person has a slow metabolism, they can have an accumulation of the drug. He said consumers can be tested for a slow metabolism.

Changes in drug sensitivity due to age

Irene is aware that as she has grown older, some additional issues have arisen due to age. One issue is that she is less able to rely on her memory, and more reliant on her diaries. The second issue is that she is aware that drug sensitivity can increase with age. As a consequence, she begins with a lower than recommended dosage of any prescribed drugs.

4.4.3.2. What problems occur when making ADR decisions?

Medical practitioner/consumer relationship

Different understandings of a set of events

In this case study, the consumer, treating medical practitioner and experts, each have very different views about Irene's condition.

According to Irene she has a significant history of reactions to medications. She maintains detailed diaries to assist in recalling the medications she has trialled, the dosages she has taken and any reactions she has experienced. She passes this information on to prescribing medical practitioners, so they can take it into account when making prescribing decisions.

Dr James said that he believes Irene had no underlying disorder that may have been responsible for the perceived hypersensitivity to drugs, apart from anxiety. According to Dr James, some of the medications taken by Irene are below a therapeutic dose, and as a consequence are unlikely to be effective. He reasoned that if she did require a lower than therapeutic dose, he would expect to see her hypertension controlled. He said, however, in the ten years of treating her, it has never been well controlled, supporting his belief that she is taking drugs at an ineffective dosage. Although not stated explicitly, Dr James appears to be suspecting that Irene is experiencing a number of nocebo effects rather than symptoms that are associated with the drugs in question.

According to one expert "it is well known that patients who develop ADRs tend to do so frequently and appear to be 'sensitive' to many drugs", and as mentioned above, she may have a slow metabolism resulting in an accumulative dosage of the drug, a characteristic that can be tested.

As can be seen, Irene and her medical practitioner, in particular, have very different understandings of what the underlying cause of Irene's apparent sensitivity to medications, and as a result make decisions based on this difference in understanding, resulting in an uncoordinated approach. Dr James indicated that his goal is to gain control of Irene's hypertension, and views her behaviour as obstructing that process by not complying with the recommended dosages. Irene indicated that she is attempting to maintain her detailed diaries, to keep information that she can pass onto prescribers to keep herself safe, due to the complexity of her case, and her own detailed knowledge of her history. She is, however, aware that medical practitioners do not always value that information. This lack of a common understanding may be contributing to the management of this condition.

Decision-making with partial knowledge

Partial knowledge of consumer and medical history

Continuing from the previous section, Dr James indicated concern about the emphasis Irene places on "illness", and felt she needed to focus on other aspects of life. When asked about the suspected reaction to hydralazine, however, Dr James was unable to state an opinion, as the case notes in his file were not summarised. Irene's detailed diaries, however, were used to locate the consultations in Dr James' medical record. Dr James upon reviewing the case notes agreed that the symptoms of lupus are likely to be associated with the drug hydralazine. He said that one of the reasons it was not suspected was because although hydralazine is associated with drug-induced lupus, it is usually at dosages significantly higher than the dosage that Irene was on, a factor that to Dr James was perplexing, but to the experts was consistent with a person with an underlying condition of increased sensitivity to medications.

In this case study, Irene has the details of dates associated with a suspected ADR, Dr James had the medical details of the episodes of care, and the experts have information about a condition that could explain Irene's condition. Each party has partial information, that when combined results in an additional possible explanation for the events.

Another issue was highlighted in this case related to partial medical history. Decision-making with only components of information may be because a person does not have access to all of the information required to make a decision. In this case, however, partial information appears to be more related to the weight placed on information that is available. As indicated above, Dr James and Irene have each interpreted the events surrounding Irene's condition differently, and so information collected by Irene is likely to be given less weight by the medical practitioner due to his understanding of the condition.

Treating medical practitioner different to the prescribing medical practitioner

In this case the specialist prescribed the drug, but the consumer initially sought treatment from a number of GPs rather than the prescribing medical practitioner. The several GPs did not detect the ADR and it was recognised by the specialist. The GP who was contacted to participate in the study stated that the specialist and he have the same information about this suspected reaction, indicating that he had received feedback from the specialist about the ADR.

4.4.4. ANALYSIS OF JOANNA'S CASE STUDY (C13)

Joanne has a significant history of allergies, in particular an anaphylactic reaction to nuts. Joanna experienced three suspected ADRs, the most severe one a suspected photosensitivity reaction to Celebrex, which resulted in ongoing photosensitivity for at least two years. Joanna's GP and the experts agree that the reaction is highly likely to be associated with the Celebrex. In this case, although Joanna was treated for the reaction in its acute phase, the association with the drug was not suspected until several weeks later, and the initial diagnosis was made by Joanna.

Joanna's specialist chose not to participate in the study, and the hospital staff were not contacted as they were outside of the ethics approval region. The details of Joanna's case study can be found in Volume two, section 1.2.4.

4.4.4.1. What problems occur when making ADR decisions?

Medical practitioner/consumer relationship

Consumer choice to accept or reject advice

Dr Casey, when making a general comment about providing ADR information to consumers, said that he believes there are problems in providing people with too much information about the possible reactions of medications. He stated that it may cause a person to choose not to take a medication, which is an important medication for their health. Joanna did not have access to information, and so she used the Internet to access the information she required in order to make a diagnosis. Joanna stated that if she were to re-live this experience, she would choose not to take the medication, but look for alternative methods of managing her injury. According to the experts, Joanna's choice not to take the medication would have been the "correct" decision for Joanna and her specialist to make, given her allergic history. This case study illustrates, not only the consumer's ability to make a diagnostic decision about a suspected ADR, but also the ability to make the decision not to take a particular medication based on preferences for treatment, and knowledge of her own case history.

Decision-making with partial knowledge

Impact of partial knowledge

Joanna stated in her interview, that she continued to take the Celebrex after the initial consultation for her symptoms in the acute phase. This implies that the treating hospital clinician either did not suspect the Celebrex as a possible cause for the reaction, or did not communicate this with Joanna. Joanna reported that she did some research on the Internet and then found listed in the product information a link between the drug and her symptoms. Although not explicitly stated, this implies that the specialist who first prescribed the reaction did not provide information about the possible reactions to the drugs prescribed.

According to the experts, if Joanna had access to that information earlier, she would have ceased the medication earlier, which may have reduced the severity of her symptoms.

Impact of no diagnosis

As stated in the previous section, Joanna continued taking the Celebrex for several weeks after the onset of the reaction, and after seeking treatment for the reaction. According to Joanna, at this stage, she was still unaware that the reaction may have been linked to the medication. It was not until several weeks later when she wondered if there was a link that she looked up the medication on the Internet. In this case, not having a diagnosis may have increased the severity of the reaction.

Advantages of sharing knowledge

Joanna's case study explores three suspected reactions. The 'facts' of the third suspected reaction were shared with Dr Carey, by the interviewer, in order to understand this suspected reaction in more detail.

In this case study, Joanna was the first to suspect the association between Flexitone and a mild skin condition. Joanna ceased the two preparations she was on at the time, the Flexitone and the beta-carotene, and then re-challenged herself with the beta-carotene, with no further reaction. She then concluded that the glucosamine within the Flexitone was responsible for the skin condition. The experts agreed with Joanna.

At the time of interview, Dr Carey was not aware of the reaction to the Flexitone. He did have some additional information that Joanna did not appear to have, however and that is that Flexitone has two key ingredients, glucosamine and Boswellia. She also did not appear to realise that a reaction may be caused by an interaction between two medications, as this did not enter into her reasoning. According to Dr Carey, it is still not known which of these two ingredients Joanna has reacted to.

Because Joanna did not share this information with Dr Carey, Dr Carey was unable to provide the additional information required by Joanna to make a complete diagnosis. Due to the mild nature of this reaction, this issue was not critical in this case, but illustrates the advantage of sharing information between consumers and medical practitioners for ADR diagnostic decision-making.

Treating medical practitioner different to the prescribing medical practitioner

This is another case study where the medical practitioner who prescribed the drug, is a different medical practitioner to the medical practitioner treating the suspected reaction. Dr Carey indicated that he was not aware that Celebrex could be associated with photosensitivity reactions, and so the act of Joanna coming to the consultation with a diagnosis meant that Dr Carey was able to make his diagnostic decision based on a clear hypothesis, rather than attempting to make a novel decision.

Complexities in the ADR decision domain

Joanna had two complexities in her case study that were not illustrated in any of the other case studies, the issue of a consumer being in a heightened state of reactivity, and the notion that there may be a hierarchy of drugs that are more or less likely to result in an ADR for consumers with particular conditions. These issues are discussed in the following two sections.

Heightened state of reactivity

Dr Carey discussed a report from the allergist. According to this report Joanna had an IGE reading of 1734 indicating an increased level of reactivity. Dr Carey said that he does not know whether this is Joanna's habitual state, or if it was raised due to one or more of the reactions. It is also unclear if the first reaction to naproxen raised Joanna's IGE levels, which resulted in an increased chance of a reaction to the second reaction, and if she had taken this medication without the initial reaction whether she would have experienced the second reaction. This case study highlights a need to understand this area, and possibly make this type of information available to prescribing medical practitioners.

Likelihood that a drug will be associated with a reaction

The second complexity is whether there is a hierarchy of drugs more likely to cause a reaction. Based on descriptions by Dr Carey and also the experts, it appears that some drugs are known to be less likely to cause a reaction. The preliminary background studies (O'Brien, 2001) highlighted the difficulty of determining the risk that any individual will experience a reaction to a drug, because not all reactions are reported, and the number of people who have taken the drug are factors that are unknown. It does appear, however, that although a percentage may not

be available to prescribers, it may be possible to develop a hierarchy of likelihood, another issue to be explored further.

Prescribing a drug which is contraindicated

In this case, Dr Carey was aware of Joanna's significant allergic history, but did not prescribe the drugs. As the specialist who prescribed the drugs did not participate in the study, it is not known if he was aware of this history. According to the experts, the class of drugs NSAIDS, should not be prescribed to a consumer with an anaphylactic reactions to nuts. Both the naproxen and the Celebrex are both drugs of this class.

4.4.4.2. How do ADRs affect people?

Impact on the medical practitioner/consumer relationship

Dr. Casey stated that in the end, nothing worked, there was no solution found to this problem, even though many paths were explored. Joanna appeared to have faith in Dr Carey, and be working co-operatively with him despite the lack of a result, indicating that a result is not the only factor a consumer requires when seeking medical treatment.

4.4.5. ANALYSIS OF PAUL'S CASE STUDY (C17)

Paul, experienced a suspected reaction to a cholesterol reducing drug, Lipitor. The low level symptoms that lasted approximately three years impacted significantly on Paul's quality of life. This case study includes the views of Paul, his GP, and two experts. The details of Paul's case can be found in Volume two, section 1.2.5.

4.4.5.1. How are ADR decisions made?

Differential diagnosis

It appears from the case study, that an ADR to the drug Lipitor was not considered in the differential diagnostic process until other diagnoses had been exhausted. Dr Kent went through a series of possible diagnoses. When Paul asked Dr Kent if he thought the symptoms may have been related to the drug, Dr Kent said that it was a possibility, but suggested exhausting other hypotheses first. It also appears from Dr Kent's interview, that he eliminated the possibility that the symptoms were related to the drug, due to the unilateral nature of the hip pain.

4.4.5.2. What problems occur when making ADR decisions?

In this case study, the suspected reaction is one that has been well documented, the mechanism for the reaction is well understood, and relatively common, yet was not detected by the medical practitioner despite a past history of an ADR to the same class of drugs. Some of the reasons for this occurring have been explored in the following sections.

Decision-making with partial knowledge

Impact of partial knowledge

Paul was not provided with information that listed the possible ADRs associated with Lipitor. He accessed information that linked the drug to the symptoms from the Internet. According to the experts, Paul should have been warned that muscle aches and pains are a common ADR to this class of drugs and if they did not go away after a while he should return for a change in drug. One expert said that "if the patient had been properly warned he would have associated the symptoms with the drug much more quickly, and the symptoms would have been recognised as an ADR sooner"

Another impact relates to sharing of knowledge between the consumer and medical practitioner. Although Paul did ask Dr Kent if he felt the symptoms could be associated with the drug on one occasion, after doing some investigations, he chose to manage the suspected ADR himself rather than discuss this with his GP. According to the experts, "more open communication" may have assisted in earlier detection of the ADR.

Consideration of test results in the context of a specific consumer

Dr Kent was aware that hepatic dysfunction is associated with this class of drugs, however decided that Paul's enzymes were not elevated significantly enough to cause suspicion. It was after Paul had ceased the Lipitor and Paul's enzymes lowered, in combination with raised cholesterol that assisted the diagnostic process.

Partial case history

In this case study, Paul previously experienced an ADR to the same class of drugs, information that possibly was in the case history. It is not known if Dr Kent had access to this information. According to the experts, the reaction could have been prevented if the fact that Paul had

previously experienced an ADR to a drug from the same class, had been taken into consideration when making the prescribing decision, and a drug from another class had been prescribed.

Complexities in the ADR decision domain

Generalised symptoms

The symptoms expressed by Paul are general symptoms that could be attributed to multiple disorders including life style. At the time of diagnosis, according to Dr Kent, Paul was in the process of changing jobs and his wife was unwell, life style factors that could also have contributed to the generalised symptoms. As a result, it is difficult to know which symptoms are part of the syndrome and which are not, especially as the problem built up over a number of years.

4.4.5.3. How do ADRs affect people?

Impact on the medical practitioner/consumer relationship

Consumer lost faith in medical practitioner

Dr Kent considered several possible diagnoses for the symptoms. When Paul suggested the possibility of an ADR, according to Paul, Dr Kent considered it briefly, but wanted to exhaust the other possibilities first. When Paul then did his own investigations, and found information that supported his hypothesis, he lost faith in his medical practitioner and decided to manage the symptoms himself rather than seek further advice from the medical practitioner. This loss of faith, which resulted in a communication breakdown, may have also delayed the detection of the ADR.

Crossing of professional boundaries

Dr Kent and Paul knew each other and were friends outside of the clinical setting. Paul and Dr Kent both spoke about whether this prior friendship may have had a negative impact on their interaction.

Paul explained that because he and Dr. Kent knew each other, they were particularly friendly, which he felt may have contributed to the communication problem. He also said that because

Paul was from the medical field, perhaps Dr Kent overestimated his knowledge and ability to make these decisions.

When asked if Dr Kent would do anything differently using the advantage of hindsight, he said that he would be more aware. He explained that he is a friend of Paul's wife, and he wondered if this relationship had an impact on hearing what Paul was saying.

Awareness of consumer experience

Dr Kent said that he believed the symptoms were not a significant problem for Paul. When asked if he would treat the situation differently if Paul had been extremely bothered by them he answered, "Yes definitely, of course I would have…" He said "it is extremely difficult to know how a consumer feels". Paul felt he had expressed the level of misery and frustration he was feeling to the medical practitioner, and felt that Dr Kent did not take the problem seriously enough. When Paul read that sometimes reactions to this class of drugs results in a permanent injury, he was even angrier that the problem was not being taken seriously enough

In this case, again a communication breakdown appeared to exacerbate the problem. Paul believed he had expressed the impact of the ADR on his life, and so needed a solution, and Dr Kent believed the problem was a small irritant to Paul, and so over time attempted to eliminate possible causes in order to manage the symptoms.

4.4.5.4. How do decision-makers contribute to new ADR knowledge?

The impact of the research process

Although Paul did not disclose to Dr Kent that he believed he had experienced a suspected ADR, the research process alerted Dr Kent to this factor. Paul provided the researchers with permission to interview his medical practitioner. Through the interview process, and the reflective thinking about the case and the advantages of hindsight, Dr Kent revised his initial diagnosis.

4.5. Case studies of suspected adverse drug reactions: low likelihood of an ADR from the consumer, medical and expert views

This section includes the second group case studies. This set of case studies include ADRs that are suspected by the consumer, however the experts believe that there is a low chance that the symptoms are associated with the drug. This set includes Kay, Mary and Tim's case studies. These cases include the consumer, medical practitioner and expert perspectives. The age range is from 29 to 70.

4.5.1. ANALYSIS OF KAY'S CASE STUDY (C05)

Kay had epilepsy, which is controlled with medication. In this case, rather than the drug in question being suspected of causing additional symptoms, Kay's suspicion, is that a generic formulation of the drug, was ineffective, and as a result she experienced a grand mal seizure, the first in 18 years. This case study includes the views of Kay the consumer, Dr. Nash Kay's regular specialist, Dr. Green the medical practitioner in the hospital, and the view of two experts. The details of Kay's case can be found in Volume two, section 1.3.1.

4.5.1.1. How are ADR decisions made?

Differential diagnosis

This case study includes the reasoning of two medical specialists and two experts regarding the differential diagnosis process that occurred in this situation. The process appeared to include holding multiple possible diagnoses, gathered information to support or eliminate each diagnosis (factors about the consumer, factors about drug behaviour, knowledge of epilepsy), considered the possible diagnoses separately, but also in combination with each other, and then eventually came to a diagnosis they believe is most likely. The other possible hypotheses do not appear to have been eliminated, but just have a lower weighting than the preferred diagnosis.

4.5.1.2. What problems occur when making ADR decisions?

Decision-making with partial knowledge

Partial knowledge of drug behaviour and ADRs

According to the medical practitioners, one method of determining the effectiveness of a drug is to measure the levels of the drug in the blood when the level is expected to be at its peak (fully absorbed). In this case, medical knowledge that was missing concerned the level of the sodium valproate in the blood serum. Dr Green determined when the blood needed to be taken for a meaningful reading, however according to Dr Green's interpretation of the medical file, they were not taken at the times requested.

Another aspect related to knowledge of ADRs. One of the experts said that the impact of a change of medication would be obvious in three to four days according to the Australian Medicine's Handbook, indicating that as the seizure occurred approximately ten days after the change of the brand of the drug, that the drug change is unlikely to be associated with the seizure.

Dr Nash said his normal procedure is to check drug levels in the blood after 14 days of commencing a new drug. According to the experts, checking after 14 days would not have detected a problem in the generic brand quickly enough to have prevented the seizure, if the problem had been the formulation of the medication.

Partial knowledge of the consumer and consumer history

It was not known by anyone whether Kay forgot her evening dose of her medication. Kay was not sure, and the level of the sodium valproate in the serum was inconclusive. Again, as a result of this lack of information, differential diagnosis was more difficult, and according to Dr Nash, not possible, as a missed dose is a hypothesis that cannot be confirmed or eliminated.

It is also unknown if in the past 18 years, whether the same set of factors, being premenstrual, sleep deprivation and alcohol have occurred at the same time in the past, to indicate if this combination may have been the cause.

Inconsistencies between decision-makers

Another factor was that according to Dr Nash, the blood levels did not drop below the therapeutic range, and he therefore eliminated the generic brand and the missed dose as probably causes. Dr Green, however, said the dose did drop below the threshold, but due to when the readings were taken, the accuracy of those results were in question.

This lack of information had an impact on differential diagnosis. According to Dr Green, it meant that it was not possible to be sure if the blood levels dropped below the therapeutic threshold, a factor which may have been able to determine if the seizure was as a result of a lower than expected drug level, or factors such as the sleep deprivation and alcohol.

Medical practitioner/consumer relationship

Differences in understanding

Kay believed that the diagnosis made by the medical practitioner was that the seizure was caused by the generic brand of Epilim, because if there was no reason for the seizure, she would have had to stop driving for three years, but because there was a reason, she only had to stop for one month. Dr Nash, however said the clear reason for the seizure, which allowed him to recommend she stops driving for one month rather than three years, was the lack of sleep.

Although Kay's explanation indicated that she believed the diagnosis was the change of brand of drug, she also appeared very shaken by the seizure, and described changes in her behaviour such as not driving if she has a lack of sleep, or if she experienced petti mals in the morning, indicating she realised the seizure may have been more related to the lack of sleep.

Complexities in the ADR decision domain

ADR resembles another disease

The primary complexity in this case was that the symptoms could have been caused by a number of factors, a "Type F" ADR, as suspected by Kay, a missed dose, or a lowering of Kay's threshold due to the factors such as a lack of sleep. There were too many unknown factors to make a diagnosis.

Reasons a consumer may choose to blame drug

One expert said that he feels that Kay may have been more prepared to accept the possibility that the seizure was caused by a drug rather than accepting that her epilepsy may be becoming more unstable.

Relationship between medical practitioner and pharmacist

One of Kay's medical practitioners mentioned that one problem in the communication between medical practitioners and pharmacists, is that some pharmacists will change a drug brand without consulting a medical practitioner, which means that the monitoring throughout the drug change cannot be performed.

4.5.2. ANALYSIS OF MARY'S CASE STUDY (C07)

Mary suspects she may have experienced a reaction to tamoxifen, a long term medication which was used to prevent the reoccurrence of cancer following a mastectomy and chemotherapy. This case study includes interviews with Mary, her specialist, Dr O'Neil and two expert views. Mary explained the events, but did not have specific dates. Dr O'Neil provided specific dates for the events described by Mary, as well as providing additional details from the case history, and his medical opinion.

In this case, Mary suspected she experienced an ADR to tamoxifen. Dr O'Neil believes the symptoms may be partially due to the tamoxifen, but primarily due to a pre-existing condition. One expert agrees with Mary, and one expert agrees with Dr O'Neil, indicating the complexity of this case. The details of Mary's case can be found in Volume two, section 1.3.2.

4.5.2.1. What problems occur when making ADR decisions?

Medical practitioner/consumer relationship

A key issue for Mary was her sense of disempowerment within the medical practitioner/consumer relationship. She mentioned several incidences of feeling "fobbed off". She also referred to other instances of care when she did not feel she was provided with information about her care that she was entitled to.

Mary decided to access information about the next drug Dr O'Neil was considering Arimidex from a hospital pharmacist.

Throughout the interview, Mary expressed feelings of anger at not being supported in her search for a diagnosis for her condition, and frustrated by the lack of information which she felt she was entitled to, at a stage when she felt too unwell to go through this process.

It is difficult to know the source of these feelings expressed by Mary. Possible sources include her frustrations of not being supported by the medical profession and family, an undiagnosed ADR, the processes described by Dr O'Neil that are associated with the realisation she had survived a life threatening illness, or depression, or some combination of these factors.

Different understandings about a set of events

There are several examples in this case study, of differences of understanding, and as a consequence, it is not possible from the information obtained in this case study, to determine a clear diagnosis. In addition to multiple possible causes of the symptoms, there were several interventions implemented within a similar time frame; the cessation of the tamoxifen, the commencement of an anti-depressant, and the commencement of psychotherapy. There are also different reports of the same events. Mary said she felt that after she came off the tamoxifen that her aches and pains were much improved, whereas Dr O'Neil said they were still there following the cessation of the tamoxifen, but ceased following the psychiatric intervention.

The experts emphasised different components of the case study. The first expert explained the aches and pains as a symptom of the depression. The second expert focused on the report that the aches and pains diminished following the cessation of the tamoxifen, and therefore associated the two.

Mary was frustrated by the lack of diagnosis, and the movement from one possible explanation to another without an explanation of all the possible causes of the symptoms, however in this case it appears it was very difficult for the medical staff to do more than work through a list of

possible causes. Possibly what Mary required was a discussion of the multiple possibilities that were being considered, so she could also work through each of them.

Complexities in the ADR decision domain

Mary's case is complex due to the number of possible factors in the equation. She has experienced a life threatening illness of cancer, and has survived, she has a history of depression, she is on multiple medications, and she has a history of musculoskeletal disorders such as a childhood accident, arthritis and degeneration of the spine. Attempting to make an association between symptoms and a cause is extremely difficult. This point is emphasised by the differences in understanding between Mary, Dr O'Neil and the two experts, and in the case study, the experts disagree on a diagnosis.

Reasons a consumer may choose to blame drug

Dr O'Neil explained that Mary may have preferred to blame the drug rather than accept her depression. At the time of Mary's interview, however, the diagnosis of depression had not been made. Dr O'Neil's interview, however, was following this diagnosis. He also said that it may have been a cry for help, and ceasing the tamoxifen as a way of indicating there was a problem that needed to be addressed.

Differences in understanding

Continuing from the previous section, the interview with Mary appeared to indicate that Mary had been trying to get help for her condition for several months, but did not feel she was being heard or taken seriously. Dr O'Neil said "I think when someone stops a drug before they see a doctor it usually means they're serious about it. So no matter what I was going to say."

4.5.3. ANALYSIS OF TIM 'S CASE STUDY (C09)

Tim made the decision to stop smoking, and used Zyban to assist with this process. Tim's case includes the consumer, medical practitioner and expert perspectives. In this case study, Tim experienced nausea and vomiting which are known 'side-effects' of the medication then developed Bell's Palsy. Both the medical practitioner and the expert believe that the Bell's Palsy was co-incidental, and unlikely to be related to the medication, however the experts stated that

they cannot be sure it is not a rare, previously unreported reaction. The details of Tim's case can be found in Volume two, section 1.3.3.

4.5.3.1. How are ADR decisions made?

Differential diagnosis

This case highlights two factors that need to be taken into consideration when making an ADR diagnosis. As highlighted in section 4.5.3.5, one of the experts highlighted the need to consider the symptoms from the drug compared with those caused by the withdrawal of nicotine. The second factor was the possibility that the Bell's Palsy occurred by chance.

The effect of the research process on decision-making

At the time of interview, Dr Price said that he did not report the suspected ADR to ADRAC as he did not believe the symptoms were associated with the drug. Using the interview to reflect back on the case, he said that using hindsight, he would report this incident in the future, because although there appeared to be no link between the two, he could not be sure.

4.5.3.2. What problems occur when making ADR decisions?

Decision-making with partial knowledge

Partial knowledge of drug behaviour and ADRs

According to Dr Price, Tim did not mention the other side effects he had experienced due to the Zyban. Tim said that he did mention the headaches and vomiting, and continued with the medication based on Dr Price's reassurances. Tim's reasoning, included his experience with the onset and cessation of the vomiting and headache which coincided with the commencement and cessation of the Zyban. Dr Price appeared to believe there was a virus also involved because Bell's Palsy is known to occur in the presence of a virus.

Another aspect of partial knowledge was that Dr Price's decision-making processes were around the assumption that when reflecting back, an ADR makes sense in some way, that is, it is related to a known pharmacological property of the drug. What he may not be aware of, is that only Type A ADRs have this characteristic, and that Type B reactions are unrelated to the drug's

known pharmacological properties. It appears from this interview that he considered the possibility that an ADR may be a Type A reaction, but not a Type B reaction.

4.6. Case studies of suspected adverse drug reactions: high likelihood of an ADR from the consumer and expert views only

This set of seven case studies includes, Julie, Belinda, Edward, James, Bob, Kerry and Robyn. aged between 35 and 70. In three of the cases, the medical practitioner chose not to participate in the study and in the remaining four cases the medical practitioners for the suspected ADRs were based in a hospital outside of the ethics approval area.

In each of these cases, at least one of the experts agreed with the consumer that there is a high likelihood that the symptoms described by the consumer were associated with the suspected drug.

As these case studies include only the consumer and expert views, most of the results emerged at the group data level, when analysing the consumer only and expert only data. The descriptions of the results of these case studies, therefore, are significantly shorter than the previous cases.

4.6.1. ANALYSIS OF JULIE'S CASE STUDY (C04)

Julie's case study illustrated the challenges of living with chronic pain, the difficulties in finding drugs or combinations of drugs that effectively manage the pain, and the increased risk of ADRs that result from particular individual drugs or interactions with drugs. Julie has a good working relationship with her medical practitioners where they work as a team to balance the risks and benefits of medications, knowing that due to the number of drugs and high doses of drugs she is taking, the goal is to minimize rather than eliminate ADRs. Julie's GP and specialist were both invited to participate in the study, but declined. The details of Julie's case can be found in Volume two, section 1.4.1.

4.6.1.1. What problems occur when making ADR decisions?

Decision-making with partial knowledge

Impact of partial knowledge

According to Julie, she requested a consumer information sheet from the pharmacist, but one was not available. A new box of medication did not include product information, she accessed the Internet and found the product information, but did not find the association. It was found that the product information did describe the suspected reaction, but it was labelled "pruritis", a name not recognised by Julie. The experts said that if she had been warned that itching may have been associated with the Tramal, the reaction may have been detected earlier.

Several times throughout the interview Julie commented on the role of information and how it allowed her to feel empowered. Without this information, she felt she had less control and limited ability to participate in discussions and decision-making with her medical practitioners.

Partial knowledge of drug behaviour and ADRs

One expert commented that rather than ceasing the Tramal, perhaps there was another antihistamine that could have been used to control the itching, but that would not have caused the drowsiness. As the expert mentioned, the GP may have had a reason for this decision, but as he chose not to participate in the interview and so his reasoning cannot be included in the study. It does highlight, however, that another source of knowledge is the knowledge of a broad range of drugs. The preliminary background studies (O'Brien, 2001) found that GPs have a group of drugs that they know well. They call this their 'preferred list' of drugs, because it is not possible to keep up to date with all of the drugs available on the market. Lack of awareness of drugs outside of the 'preferred list' may be another source of partial knowledge.

Complexities in the ADR decision domain

Julie's complex case history increases the difficulty of prescribing decisions. Below are two examples.

Weighing risk versus benefit of drug therapy

The ADR to Tramal was treated with Periactin. Julie then experienced a second ADR to the Periactin. According to the experts, if the initial ADR had not been treated with a drug, the

second ADR would not have occurred. In this case, however, the benefits of the Tramal were so significant to Julie, that treating the ADR was preferable to ceasing the medication.

Multiple medications

Julie has a history which includes chronic pain, psychological issues and polycystic ovary syndrome, and is therefore on multiple medications all of the time. Management of the pain is difficult, and so combinations of medications are often trialled. When trialling a new combination of drugs, Julie and her medical practitioner do not expect to eliminate ADR completely, but aim to maximize the therapeutic benefits whilst minimizing the ADRs.

4.6.2. ANALYSIS OF BELINDA'S CASE STUDY (C08)

Belinda whilst having knee surgery under an epidural, experienced a very slow heartbeat, felt "spaced out" and was very cold, a reaction she believes, to the Inderal, symptoms which lasted three days.

Belinda's surgery occurred in a hospital outside of the area studied, and so the medical practitioners were not contacted for medical records. Belinda also saw a GP who assisted in the management of her migraines, who was contacted to participate in the study, however he did not respond to the request. This case study therefore includes only Belinda and the expert views. The experts both agree that there was a likely interaction between the Inderal and one or more of the drugs used during the surgery, resulting in bradycardia, dissociation and anomia but without access to the medical record were unable to determine which drugs were involved. The details of Belinda's case can be found in Volume two, section 1.4.2.

4.6.2.1. How are ADR decisions made?

Prescribing decisions

Accurate drug history information

This study illustrates the difficulties in making a diagnosis without information about drug/s and dosages, and consumer information such as age, body weight. In this case study, the consumer was able to provide detailed information about her experience, but did not have the details of her case history.

4.6.2.2. What problems occur when making ADR decisions?

Decision-making with partial knowledge

Prevention of future ADRs

As a diagnosis has not been made, if Belinda were to have further surgery future medical practitioners would also not be able to use this information to prevent future ADRs. Because Belinda does not have this information and unless she went to the same hospital, the information would not be available in order to prevent the reaction happening a second time. Because Belinda was concerned about future surgery, she chose to work with her GP to cease the Inderal.

Partial knowledge of drug behaviour and ADRs

According to the experts, the staff treating Belinda did not appear to be aware of the potential ADRs associated with beta blockers, prior to the surgery, and so according to Belinda, did not determine the reason for her symptoms immediately.

4.6.3. ANALYSIS OF EDWARD'S CASE STUDY (C10)

In this case there is a clear temporal link between the drug and the reaction, especially because when Edward took the drug a second time he experienced the same reaction a second time (referred to by medical practitioners as a rechallenge). The unique aspect of this case is that the impact was more severe due to the context of Edward's life, rather than the immediate effects of the ADR.

Edward's GP chose not to participate in the study. The message conveyed by the medical practitioner's receptionist was that even though Edward had given his permission for the medical practitioner to discuss the case, he was not prepared to as he felt the study was an invasion of the medical practitioner/consumer relationship. The details of Edward's case can be found in Volume two, section 1.4.3.

4.6.3.1. What problems occur when making ADR decisions?

Decision-making with partial knowledge

Management of ADRs

In this case, the management of the ADR was rest. The experts stated that another medication could have been used in an attempt to stop the second bout of vomiting, however Edward believed that if the Stemetil had not stopped the vomiting, other medications would also be ineffective. One expert said that hospitalisation would be expected because of the risk of renal failure and dehydration, in a person of Edward's age. As the medical practitioner was not interviewed, the reasoning behind this decision is not available.

Partial knowledge of drug behaviour and ADRs

Edward attributed all of his symptoms to the ADR. The experts said that the initial vomiting had a high probability of being associated with the drug, but the prolonged vomiting was probably caused by another illness.

Impact of partial knowledge

If Edward had been aware that a second dose of the drug may have caused a second bout of the vomiting, he stated that he would not have chosen to take a second dose, a decision that would have prevented the second ADR. According to one expert, there was a high probability that the second dose would result in a second bout of vomiting. The lack of information impeded Edward's ability to make a decision that would have prevented the ADR.

4.6.4. ANALYSIS OF JAMES' CASE STUDY (C12)

James experienced a series of suspected reactions that occurred over several years in hospitals outside of the study region. As he did not report these symptoms and suspicion of ADR to the hospitals or his GP, the medical staff were not contacted to participate in the study.

This is the only case where the diagnostic decision-making was made entirely by the consumer with no input from medical practitioners. The details of James' case can be found in Volume two, section 1.4.4.

As this case study includes primarily the consumer view, most of the results of this case study have been reported in the combined group analysis in chapter five. The only additional result from this case study is one about partial knowledge, below.

4.6.4.1. What problems occur when making ADR decisions?
Decision-making with partial knowledge

Partial knowledge of drug behaviour and ADRs

James made the differential diagnosis himself, a diagnostic decision that was supported by the experts. James said that he would have liked to have been warned that it is possible to have reactions to medications, so that this information could have been taken into consideration in his own decision-making.

4.6.5. ANALYSIS OF BOB'S CASE STUDY (C14)

Bob experienced a suspected ADR to Vioxx, in the form of a mild photosensitivity reaction. It was over time that Bob noticed the association between the sun and the redness and itching, but at the time of interview, he was attempting to establish if there was a link between the symptoms and the rash. Bob's GP chose not to participate in the study. One expert believes there is a high likelihood that the symptoms are associated with the drug, and the second expert believes there is a very low likelihood of an association. The details of Bob's case can be found in Volume two, section 1.4.5.

4.6.5.1. What problems occur when making ADR decisions?
Decision-making with partial knowledge

Impact of no diagnosis

Due to the irritating nature of this reaction, Bob initially requested advice from his medical practitioner, but eventually concluded, "he probably won't know." He then went on to access information from his wife, his wife's cousin, his daughter, the family pharmacist, and then chose to participate in this study in an attempt to gather further information. His medical practitioner suggested he stop the Vioxx, which according to Bob he had already done, and suggested some treatments that Bob did not feel were practical or effective.

4.6.5.2. How do ADRs affect people?

Impact of an ADR

Mild but irritating reaction

Although this ADR was relatively mild, it appeared to be causing Bob significant annoyance, possibly due to not knowing what was causing it, and also, because of the impact it was having on his enjoyment of outdoor or recreational activities. This was illustrated when Bob said " I work inside all the time and I like to…I don't like extreme hot weather, but I like to get out. Like I said, I do a bit of fishing and that. I like to get the shorts on and all that…"

Impact on medical practitioner/consumer relationship

As a consequence of this consultation, Bob appeared to loose faith in his medical practitioner. The fact that the two experts disagreed on a likely diagnosis for the symptoms indicates that this case is difficult to diagnose, so even though the GP attempted to manage the ADR, the lack of diagnosis appeared to be the key issue.

When the transcript was sent to Bob for verification, he telephoned to report some additional information about his case. He said that his medical practitioner at that stage suspected an environmental irritant in Bob's work place and was investigating that further. No additional information about this was provided by Bob. Bob's medical practitioner chose not to participate in the study, and so no further information was accessible via him either.

4.6.6. ANALYSIS OF KERRY'S CASE STUDY (C15)

In this case study, the particular ADR described in the case study, and Kerry's history of ADRs are all associated with the experience of anaesthetic drugs and surgery. The cumulative effect of multiple ADRs has been a fear of surgery, limiting Kerry's therapeutic choices in the future.

The ADR reported in this case study occurred in a hospital outside of the study region, and so the medical practitioners were not contacted for their input into the study. The experts agree that there is a moderate likelihood that the drug Maxolon is associated with the symptoms of visual disturbances. The details of Kerry's case can be found in Volume two, section 1.4.6.

4.6.6.1. How are ADR decisions made?

Differential diagnosis

In this case, there were multiple events occurring at the same time, making it difficult to determine which drug was responsible for the visual disturbances. The experts used factors outside the case study situation, such as other case studies in the ADRAC database, and the history of anaesthetics without this particular reaction to hypothesis about which agent was most likely responsible for the reaction.

4.6.6.2. What are the problems when making ADR decisions?

Impact of partial knowledge

Kerry expressed fear associated with surgery based on her complex medical history and several ADRs following surgery. She wanted to discuss her concerns with the anaesthetists prior to surgery, but found she was unable to due to the time the medical practitioners had available. The inability to discuss the procedures prior to the surgery, and her history of ADRs related to anaesthetic drugs, added to her anxiety and fear of future surgery.

Partial knowledge of consumer and consumer history

Kerry has had several operations at various hospitals. Her medical file, therefore is spread over multiple sites. Kerry has a lay person's view of what happened, but it appears that each time she has another operation, she needs to spend time passing on her complex history to the new team of medical practitioners. Within this single interview, there are inconsistencies in what Kerry describes, indicating that she is not clear herself what happened post surgery, and appeared to be attempting to make sense of what happened.

4.6.6.3. How ADRs affect people?

Impact of ADR

This is another ADR where the impact is more significant than the immediate impact. In this case, the ADR is added to other negative experiences, resulting in Kerry being extremely fearful of anaesthetics. As explained by the expert, when a person is unable to use a particular drug or undertake particular interventions, their options are restricted.

An additional outcome of this reaction expressed by one of the experts is that "this experience has reinforced her fear of surgery and anaesthesia, which may have the effect of further limiting future therapeutic options."

4.6.7. ANALYSIS OF JOAN'S CASE STUDY (C16)

Joan heard about this study and volunteered even though she lived outside the study area. The interview was conducted via telephone. When the transcript was sent back to Joan, she chose to type her response to the questions and asked for her written interview to be used rather than the verbal one.

Joan has severe epilepsy which has been difficult to control. When the epilepsy is not controlled she has periods of time when she is not aware of what she is doing or where she is going. The ADR she described in this case study occurred when Joan's husband, Ron, was at home. Joan was in an altered state of consciousness at the time of the suspected ADR, and therefore suggested Ron be interviewed as well. This case study, therefore, includes the consumer view, and also the view of her husband. The details of Joan's case can be found in Volume two, section 1.4.7.

4.6.7.1. How are ADR decisions made?

Differential diagnosis

ADR resembles the pre-existing disease

This case study illustrates the complexity of differentially diagnosing ADRs when there are multiple medications, and where the symptoms from the ADR are similar to a worsening pre-existing condition.

Weighing risks versus benefit

According to the experts, the commencement of the drug Sabril was temporally related to the symptoms described by Joan. The condition worsened because of the medical decision to continue with the drug, despite Joan's reports of worsening symptoms as the dose increased. According to Joan, the medical decision was based on another case where the Sabril improved

another consumer's condition significantly, a consumer with an apparently similar profile to Joan's. In this case, the medical practitioner, weighing up the risks and benefits appeared to be putting a significant weight on the possible positive benefits of the Sabril, compared with the risks of the ADR. It was when Joan decided that the risks outweighed the potential benefits that the drug was ceased.

4.6.7.2. What Problems occur when making ADR decisions?

Decisions that may contribute to an ADR

According to the experts, one reason why the Tegretol was not detected as contributing to the problem in controlling the epilepsy earlier, was because Joan chose not to participate in "video monitoring" assessment, where all drugs are withdrawn and then gradually introduced under controlled conditions.

In this case, the ADR, rather than producing the required effect, produced an unwanted reaction, actually produced the opposite effect from what was expected from the drug. Rather than reducing the epilepsy, it made it worse.

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4.7. Conclusion

Analysis of 15 individual case studies has been presented in this chapter, eight that include the consumer, medical practitioner and expert perspectives, and seven that include only the consumer and medical practitioner perspectives.

The first set of five case studies included the consumer, medical practitioner and expert view, and each participant agreed that there was a high likelihood that the symptoms were associated with the suspected drug/s. The second set of three case studies, included all three perspectives again, but the experts believe there is a low likelihood that the suspected drug was associated with the consumer's symptoms. The final set included only the consumer and expert perspectives, and in each of these cases, the experts agreed that there is a likelihood that the symptoms are associated with the suspected drug.

As can be seen from the summaries of each section, a large number of results have emerged from this method of analysis. Below are the key results:

- Diagnostic processes included the use of pattern matching or recognition that a set of symptoms are associated with a medication due to past experience, hypothesising a number of possible diagnoses, and using knowledge and information sources to alter the weights associated with each possible diagnosis and logic and reasoning including the temporal relationship between the commencement of a drug and the onset of the new symptoms. In some cases an ADR was in the list of possible hypotheses, and in other cases it was not considered until later in the diagnostic process.

- For each of the case studies that did not include a medical practitioner perspective, at least one expert agreed that the symptoms were likely to be associated with an ADR, strengthening the view that consumers can play an important role in the reporting of ADRs. In many of the case studies, the consumer was the first to detect the suspected ADR, and in most of these cases the experts agreed with this diagnosis. This indicates that consumers play an important role in the detection of ADRs.

- The largest problem in the ADR decision domain highlighted by this set of data, and not seen from the group data analysis, was the issue of partial knowledge. Each of the participants held a particular set of knowledge and accessed information from multiple sources. The consumers had knowledge of their own body, awareness of what is in their medical history, and awareness of their own preferences. The medical practitioners had expertise in disease diagnosis and management, and access to information about the consumer contained in the medical file and shared by the consumer, and some knowledge of drugs. The experts had expertise in drugs and ADRs, and access to the content of the case studies. The pharmacists knowledge was often not included. A theme arising from these data is that access to only a component of the knowledge and information available relating to the suspected ADR appeared to contribute to the incidence, and delayed detection of ADRs.

- An emerging theme relating to the consequences of decision-making using partial knowledge related to the consumer's ability to participate in decision-making. A lack of information about potential ADRs made it difficult for the consumers to participate in the ADR decision-making, resulting in either a prolonged ADR or impeding the consumer's ability to make an informed decision about whether or not to take a medication.

- New knowledge about ADRs is created at a national level through spontaneous reporting and at an individual level by accessing national and international data, but also through personal experience. An emerging theme from these data was that the medical practitioner did not receive feedback that a drug they prescribed resulted in a suspected ADR, inhibiting individual learning. In two cases the research process of using reflective thinking assisted the medical practitioners to re-evaluate their decisions and change their conclusions.

The following chapter includes the results from the group analysis and from the analysis combining the group and individual case study analysis.

CHAPTER FIVE

Results: Group Analysis and Combined Methods Case Study Analysis

5.1. Introduction

The previous chapter presented the analysis of the data at an individual case study level. This chapter presents the results that emerged when viewing the data at a group level, that is the consumers as a group, the medical practitioners as a group and the experts as a group.

As described in the chapter three, one aim of using several methods of analysis was to extract the maximum from the data, but present them with minimal repetition. Following the group analysis is a section which presents the results obtained combining the group and individual case study data together.

The structure of this chapter is similar to that of the previous chapter. Again, research questions have been used to structure each section, and the key themes that have emerged that relate to each research question are used as subsections.

5.2. Group analysis - Consumer view

The consumer group analysis included the analysis of the consumer interviews in isolation without considering the medical practitioner or expert perspectives. This analysis, therefore, includes the 15 consumer interviews, and also includes the interview of Joan's husband, Ron as Joan was not fully conscious of what happened during her suspected ADR.

5.2.1. WHO ARE THE DECISION-MAKERS IN THE ADR DOMAIN?

A key aspect of this exploratory research is to understand more about the decision processes surrounding ADRs. A logical question, therefore, is who are the decision-makers within this domain? As described in the review of the literature (chapter two), the majority of decision support has been developed for the medical practitioner, however the preliminary background studies (O'Brien & Yearwood, 2002) indicated that there may be others involved in the decision-making processes surrounding ADRs. The consumer data provided the following insights.

5.2.1.1. Multiple decision-makers

Within the 15 case studies, according to the consumers, the people involved in decision-making (either making decisions or providing observational input into the decision-making) included, the prescriber who was either the GP or a specialist, the consumer, members of the consumer's family and the consumer's friends, the pharmacist and/or other health professionals such as a naturopath. Table 5-1 describes for each of the suspected ADRs, the symptoms, suspected drug, level of certainty that the drug is associated with the symptoms, the sources of knowledge used to make the diagnosis, who make the diagnosis and the impact of the suspected ADR, all from the consumer only perspective. As will become clear later in this chapter, the medical practitioners and experts did not agree with these forms of analysis in all cases. Table 5-1, column five shows that from the consumer's perspective, the consumer was involved in the diagnostic decision-making process; one type of decision-making, in 11 of the 15 cases and in seven of the 15 cases described this decision as collaborative. The collaboration is with a family member in four of these cases and with the medical practitioner in three cases.

5.2.2. WHAT DECISIONS ARE MADE BY EACH DECISION-MAKER?

5.2.2.1. Types of decisions made by consumers

Table 5-1 above, explores the diagnostic decision type of "suspecting a drug to have caused a reaction". Other decisions made by the consumers within these 15 cases are described in Table 5-2.

Consumer Code	Symptoms	Drug	Level of Certainty	Source of knowledge used by consumer and medical practitioner as perceived by consumer.	Who diagnosed	Impact
Toni C02	Severe influenza style illness	Tegretol	High	GP consulted specialist	Medical practitioner	"I really felt like I couldn't drive, I was feeling really miserable." "he said (GP) "you are seriously ill""
Julie C04	Itchy in absence of rash	tramadol hydro-chloride	High	Internet, observation and asking the medical practitioner.	Medical practitioner	Concerned and confused not knowing the cause
Kay C05	Grand Mal first for 18 years.	Generic brand of sodium valproate	Consumer High	Elimination of other possible factors	Consumer and medical practitioner	"the impact for me personally was huge"
Helen C06	Convulsions	Panadeine Forte	Medium	Advice from medical practitioner	Medical practitioner	"I won't take it again, just in case."
Mary C07	Aches in legs, nausea	tamoxifen	High	Consumer's reflection and specialist's medical knowledge	Consumer suspected medication and the medical practitioner confirmed	"I just felt I was getting weaker and sicker and I was angry by this stage too…I felt that I was bit fobbed off'
Belinda C08	Slow recovery from epidural	Inderal	Medium	Observation and prior knowledge of medication.	Consumer and GP suspected	"I don't want to be prescribed drugs again if it's not necessary."
Tim C09	Bell's Palsy	Zyban	Mod High	Observation and elimination of other possibilities.	Consumer	"I was nearly in tears, I didn't know what was wrong"
Edward C10	Vomiting after second dose for two weeks	Efexor	High	Symptoms immediately following taking the drug. Re- challenged	Consumer, confirmed by GP	"Nobody on earth could talk me into trying it again."

Irene C11	Drug induced lupus	hydralazine	High	Observation, Internet.	Consumer, confirmed by medical practitioner.	"I was just in agony"
James C12	Felt ill enough to miss work.	Panadeine Forte	High	Observation. Several uses over time.	Consumer and wife	"It delayed my return to work"
Joanna C13	Photo-sensitivity – pustule rash	Celebrex	High	Observation and the Internet	Consumer	"The impact was major. For the period of the reaction I was miserable."
Bob C14	Photo-sensitivity – itchy rash	Vioxx	Low	Observation and information from friends	Consumer, wife, wife's cousin and daughter.	Searching for an explanation for the symptoms for 18 months.
Kerry C15	Double vision	Maxolon	High	Medical practitioner referred to ADR reference material.	Medical practitioner	"I'm terrified of having any more surgery absolutely terrified" (after a series of unpredictable reactions to drugs)
Robyn C16	Induced severe seizure – similar to psychotic episode.	Sabril	High	Timing of medication with suspected reaction.	Consumer and husband	"was terrifying" "It did shatter me psychologically"
Paul C17	Restless Legs, unwell, pain in legs	Lipitor	High	Observation by the consumer and his wife, own medical knowledge, Internet.	Consumer	"I'm miserable…. [its] the decrease in the quality of life"

Table 5-1 Detecting suspected ADRs from a consumer's perspective

These consumer data indicate that consumers are involved in a wide range of decisions surrounding suspected ADRs, broader than the treatment decisions and diagnostic decisions discussed in the literature review (sections 2.3.2 and 2.3.3). These results also indicate that the decision types made by consumers are significantly broader than the current ADR decision support focus.

Decision Type	Decisions made by consumers
Diagnostic decisions	Suspect a drug of causing a reaction
	Suspect a class of drugs of causing a reaction.
	When given a diagnosis by a medical practitioner, whether to accept the diagnosis
Treatment decisions	Whether to use drug therapy
	Which medication to take – prescription, non prescription or complementary
	Whether to take prescribed medication
	To take a medication prescribed for a family member or friend.
	Decision to request a specific drug from a medical practitioner
	Decision between multiple suitable drugs
	Decision to take medication prescribed for self, for a previous illness.
	When to begin or cease a drug.
	Frequency of drug
	Whether to follow recommendations by medical practitioner or product information.
	Whether to accept a side effect because of the benefits of the medication.
Information sharing	Whether to report a suspected reaction to a medication practitioner
	Whether to report new symptoms to a medical practitioner
	Which information to share with a medical practitioner
	Whether to request specific information about a drug
	Determine the priority for treatment
	Inform medical practitioner of ceasing a medication
	Inform a medical practitioner of 'non-compliance' – eg higher dose than recommended.
	When to report a suspected reaction to a medical practitioner
Seeking information	Who to seek information from; medical practitioner, pharmacist, naturopath, friend, family
	When to seek information.
	Where to seek information – Internet, person, media, drug product information

Table 5-2 Decisions made by consumers during a suspected ADR from a consumer perspective

5.2.2.2. Consumers as diagnostic decision-makers

As described in chapter two, the majority of decision support has focused on the prescriber, and decision support that includes consumers is mainly for treatment decisions. These consumer data revealed that in 11 of the 15 cases, the consumer was involved in the diagnostic decision-

making process. In seven of those 11 cases, the consumer believes that s/he made the diagnosis without the assistance of the medical practitioner. (O'Brien & Yearwood, 2003)

5.2.2.3. The role of the pharmacist

Three case studies included the role of the pharmacist in ADR decision-making. The decision types made by the pharmacist are listed in Table 5-3 below.

Pharmacist decision	Case study
Recommend changing drug from branded drug to generic.	Kay
Provided information about drug properties	Kay
Provided information about potential ADRs associated with drugs	Julie
Advised consumer to seek medical assistance	Toni

Table 5-3 ADR decisions made by pharmacists

5.2.3. WHAT DO DECISION-MAKERS UNDERSTAND BY THE TERM ADR?

The terms side effect, reaction and allergy have all been used by the consumers in the interviews. It is not the intention of this study to do an in-depth linguistic analysis of the use of these terms, however some understanding of how people use particular terms is important in order to understand their intention.

A direct question about the difference in meaning between side-effect and reaction was not asked to many consumers, and many of those who were asked, did not appear to have a clear explanation. One participant, however, offered an explanation of her understanding of the term 'side effects':

> I suppose I don't see side effects as necessarily being that negative if you can cope with it…I mean if it's a side effect it's, I think if it can be handled otherwise I don't necessarily see it as negative because it's just part of it…

Another method of determining the meaning attributed to these terms is to observe how the term is used in conversation. One pattern that appeared to emerge where the term 'side effect' was primarily used to refer to an attribute of the drug, where as the term 'reaction' appeared to be used to refer to the experience of the consumer. Another pattern was the combined use of 'side effect' and 'reaction'. Reaction was used as something more severe than a side effect that was unexpected and more severe.

5.2.3.1. 'Side effect' as an attribute of a drug

The following extracts illustrate the use of the term 'side effect' as an attribute of the drug:

> I'd be discussing probably now [following the suspected ADR] with my GP what the options are and going through all the side effects.

> …looking up the [drug] on the computer wondering what sort of side effects it had.

> So he called me on a Saturday morning and said I will send you a prescription and you can start taking that and I said are there any side effects…

> No [I didn't see the Dr] because it's, headaches are one of the side effects of [the drug] is throwing up, it's, they were both side effects of [the drug]

> They list every conceivable side effect that anyone's ever had.

In each of these cases 'side effect' was used as a general term which did not appear to reflect severity.

5.2.3.2. 'Side effect' as an expected but non-therapeutic effect of the drug

In the examples below, the consumer has experienced symptoms s/he has attributed to non therapeutic effects of the drug that do not appear to be of a major concern to the consumer, possibly because the cause of the symptoms is known. In these examples, the term 'side effect' is still used as an attribute of the drug, but as can be seen, the side effect appears to be something that is expected, by at least one party, either the consumer, medical practitioner and/or documented in the product information:

> I was experiencing very severe headaches, migraines averaging about one to two a week and I was throwing up about once a week and I continued with it, the doctor said no, no, no that's all right it's just side effects [of the drug] so I continued.

> I told the doctor I was getting bad dreams and apparently that is one of the side effects of it [the drug].

5.2.3.3. 'Reaction' describing the experience of the consumer

The term 'reaction' appeared to be the term most often used when referring to the consumer's experience of the symptoms. Some examples follow:

> …just because on a previous occasion I had a bad reaction.

> I mean it wasn't that I has having fever or anything I was simply throwing up and I was getting headaches and it was the fact that was happening so regularly over the period that to me said it wasn't so much a viral infection I was just having a normal reaction to the drug.

> Well I have a reaction to a lot of things.

> …if somewhere the fact that some people have a reaction to either Panadeine Forte or Tramal or whatever it might be would be useful to know that so it could be taken into consideration.

This use of the term 'reaction' did not appear to be related to the severity or whether the symptoms were expected. It seemed to be used generally to indicate the person's experience.

5.2.3.4. 'Allergy' as a type of reaction

The term 'allergy' was used by eight of the consumers. In the majority of cases, the consumer had been told by a medical practitioner that s/he had an allergy, and so used the same term. Edward used the term 'allergy' as a term meaning 'reaction' Other consumers appeared to use the term as a subtype of allergy, which is consistent with the expert definition. Some examples have been listed below:

> I must be allergic to Codeine.

> …[the] doctor has said that it was an allergic reaction and to stay off the [drug].

> I had an allergic reaction.

> Whether if I'd gone to casualty they might have given me Maxolon or something else that might have worked I don't know. I got the impression not. You're stuck with a total allergy…Well again, if I got an allergic reaction like that nobody on earth could talk me into trying it again.

> As a child I had an allergy to eggs.

> I think he also did a blood test if I remember and it did show that I could have had an allergy but he thought it was more like an environmental allergy.

5.2.3.5. Terminology used when quoting a health professional

At times the consumer referred to a diagnosis made by a medical practitioner. In these cases, it appears that the consumer uses the terminology used by the medical practitioner. As it is not possible to know what terminology was used by the medical practitioner, this can only be a suggestion at this stage:

> [Quoting a medical practitioner in an emergency clinic] "I know what you've come for, you've got an allergy to…", that was a definite allergy.

The other possible complexity related to the use of terminology, is that the term 'reaction' or 'suspected reaction' was used consistently by the interviewer throughout the interview process. It is possible that the consumers, having answered an advertisement for people who believe they may have experienced an adverse drug reaction, to have adopted this terminology for the purposes of the study.

5.2.4. WHAT PROBLEMS OCCUR WHEN MAKING ADR DECISIONS?

5.2.4.1. Medical practitioner/consumer relationship

Responsibility of health care

The consumer group raised concerns about their care throughout their suspected ADR. Using hindsight, they would have liked the following changes in their care. They would have liked:

- not be told, do not worry, it is nothing to worry about, it will pass;

- additional information about the suspected ADR to assist with giving the consumer ownership of their condition;
- for the medical practitioner to take more responsibility for ensuring diagnosis is correct;
- for the medical practitioner to not take responsibility for what the consumer does or does not need to know;
- for the medical practitioner not to patronize;
- for the medical practitioner to take this information the consumer had collected about her own experiences into consideration when making future treatment recommendations.

The consumer choice to accept or reject advice

Several consumers said that using hindsight they would not necessarily have followed the advice given by the medical practitioner, or may have requested more information to clarify the recommendation before making a decision about whether to follow it or not.

- one consumer said he would not have taken the medical practitioner's advice to take a second tablet when there had been a significant reaction to the first dosage;
- two consumers said they would not have taken a non-essential medication. These consumers would have looked for an alternative to drug treatment,
- one comment was that agreeing to take a medication means fully understanding the possible consequences of this agreement. This consumer said she needed to know more about what she was agreeing to regarding drug treatments;
- one consumer would not have taken the generic brand of a medication suggested by the pharmacist.

Consumer satisfaction with episode/s of care surrounding suspected ADR

When asked, again using hindsight, what the consumers would have liked their medical practitioner to have done differently, there were many positive comments from the consumer group. Two have been listed below:

> I know from past experience if my GP's felt he hasn't been able to cope with the situations he's … sent me back to [Perth] so I suppose when you know he was clear about this well

> you know it's not like I had to question whether you know he wouldn't do the best for me because I knew he would and I knew that he would send me back to [the specialist] if there wasn't anything that could be done.
>
> …even the GP was because of the high temperature was saying I don't think it can be and you know then went ahead and checked it up and realised it was. I mean he'd told me to come off it already so he was terrific).

One issue raised by several consumers was the issue of access to information. Eight of the consumers expressed a desire for more information about possible reactions to drugs, or about disease and disease processes. Following are two lists, the first is a list of information the consumers would have liked access to about drugs, and the second about diseases.

5.2.4.2. Decision-making with partial knowledge

Information about drugs and ADRs

A discussion of the differences between information and knowledge can be found in section 2.3.4.4. This section refers to information sources the consumer's would have liked. The consumer group indicated that they would have liked access to the following information about drugs and potential ADRs. These included:

- a discussion of possible side effects to a drug prescribed for them;
- warnings of what to look out for and when to seek medical treatment, particularly when a potential reaction could look like another common illness;
- written information about possible ADRs using common language that is easy to understand without technical jargon, from either the medical practitioner or pharmacist For example, pruritis = itchiness, but the consumer did not recognise it as such;
- clear information about the positive and negative effects of drugs so consent to take the medication is informed;
- an explanation of the cause of new symptoms and the likely course of the suspected reaction, as it is likely to be a disease process not previously experienced by the consumers.

Information about disease and treatment options

The consumer group indicated that they would have liked access to the following information about diseases and treatment options. These included:

- a warning that post-surgery the consumer may feel unwell and therefore need medication, allowing the consumer to plan and purchase a suitable drug rather than take an inappropriate drug that was readily available;
- all of the possible sources of the symptoms rather than just providing a single suggestion, so the consumer is aware of what options are being considered;
- information about what is likely to happen during a surgical procedure.

As can be seen from section 5.2.2, consumers in this study were actively involved in making a wide variety of decisions within this domain and without information this task was more difficult. At the time of the suspected ADR, the consumer may not have realised it was required, in retrospect they see it would have been useful. It is also about providing information that is directly requested by the consumer using language that is understandable by the consumer. In several cases when information was requested directly, it was not provided.

5.2.4.3. Decisions that may contribute to an ADR

Ignoring recommended dose

In two cases, the consumers chose to ignore the recommended dose of a medication that may have contributed to the prolongation of their ADRs.

Julie initially chose not to tell her GP that she was taking a higher than recommended dose of the Periactin to manage the ADR to Tramal, because the Tramal was the only drug she had found that managed the pain and did not cause drowsiness. She was concerned that informing her medical practitioner would mean that she would have to stop the Tramal which she found very effective in managing her pain. Taking a higher than recommended dose of the Periactin to assist with the management of the initial ADR, resulted in a second ADR , one which is a Type A reaction which is dose related. The second ADR, therefore, was unlikely to have occurred if Julie had not exceeded the dosage.

Toni chose to take a higher dosage of Aspro Clear than was recommended to manage the increasingly severe symptoms due to high work and family commitments. At the time, she believed she had a cold or flu, a disease she was familiar with. Her decision to seek medical assistance was delayed due to her choice to put family and work commitments before her health. This delay in seeking medical treatment may have resulted in a delay in diagnosis of the ADR.

Decision not to share information with medical practitioner

In six case studies, the consumer chose not to share information with either the medical practitioner or the prescribing clinician. In two cases, the consumer was prescribed the drug by one medical practitioner, but another medical practitioner was the treating medical practitioner, and so the consumer did not have a reason to speak with the prescribing medical practitioner. In two more cases, the suspected ADR occurred post surgery, but because there was not surgical follow up consultation, again, there was no reason for the consumer to make an appointment with the prescribing clinician. In one case, the consumer lost confidence in the medical practitioner and so decided not to go back, and in the final case, the consumer did not want to share with the prescriber that she was experiencing an ADR, because the medication was working well in treating the original condition.

5.2.4.4. Complexities in the ADR decision domain

Essential versus non-essential medications

In most of the case studies, the medication taken by the consumer was a non-essential medication, and so the decision to cease the medication was not critical. In Joan's case, medication is essential for controlling her pre-existing condition of epilepsy, and so the decision to cease one medication, meant that another medication was needed to replace it immediately, making the decision to cease a medication more complex. In contrast, the medications taken by James were non-essential medications and the symptoms were not severe, and so the risks associated with this diagnostic decision were low.

5.2.5. WHAT RESOURCES ARE USED BY DECISION-MAKERS?

5.2.5.1. Information, knowledge sources and content used by the consumers

Information and sources of knowledge that were used by the consumers when making decisions surrounding ADRs were extracted from the interviews during the coding process. Below are

three lists, one of information sources used, and the second of knowledge sources used and the third one the types of information gathered.

The sources of **information** used by the consumers included:

- the product information sheet;
- consumer drug information sheet from the pharmacist;
- personal diaries;
- the Internet;
- advice from medical practitioner;
- advice from a family member;
- observations of self;
- family and friend's observations of consumer's symptoms;
- family and friend's recollections of past events;
- hearing about case studies similar to own;
- family friends;
- the pharmacist.

Sources of **knowledge** used by the consumers included:

- past experience with medicines;
- past experience with particular diseases, including suspected ADRs;
- their own behaviour surrounding medications such as when medications were commenced and/or ceased.

Content of information and knowledge used by the consumers:

- general information about drugs;
- general information about diseases;
- classes of drugs;
- alternative drugs for a similar treatment;
- potential ADRs associated with drugs;
- dosage;

- time required for medication to reach therapeutic level;
- characteristics of own body.

As can be seen by the lists above, the consumer group accessed information from a variety of sources and on several topics, as well as accessing their own knowledge. Only one source of information was from a medical practitioner.

5.2.6. HOW DO ADRS AFFECT CONSUMERS AND HOW DOES THIS IMPACT ON FUTURE DECISION-MAKING?

A component of gaining insight into ADRs, is to understand the impact they have on a person's life. This section discusses three key themes that emerged on this topic. Section 5.2.6.1 explores the consumers' perception of the severity of their ADR experience, section 5.2.6.2 discusses the importance of including a life context when attempting to understand the impact of ADRs, and finally section 5.2.6.3 looks at the impact of experiencing symptoms that the consumer expected versus those that were totally unexpected.

5.2.6.1. Perception of the severity of suspected ADRs

Although the suspected reactions reported by the consumers are not life threatening and did not cause death or permanent physical injury, each consumer found the suspected reaction distressing. The impact of the ADRs as described by the consumers appeared to fall into five key categories: the immediate impact of a suspected ADR; the impact after a drug has been ceased; the impact on the medical practitioner/consumer relationship; the impact on trust; and finally the impact on lifestyle.

Immediate impact of a suspected ADR

The first two quotes, below, indicate the impact on the consumer whilst experiencing the suspected reaction:

> I got home but I had to go to work for half an hour so my husband was going to drive me there because I really felt like I couldn't drive, I was feeling really miserable.

> I said [to GP] I'm miserable, I said my legs, I said I've got pain, I've got this restless legs, I've got this thigh pain around here and stuff like that and I said I'm miserable you know I really am. Is this the way life's supposed to be?

Toni had eight weeks of illness and said she didn't feel completely well again for ten weeks. Paul indicated that the symptoms had persisted for three years progressively getting worse.

Impact of a suspected ADR after the drug has been ceased

The following quote indicates how a suspected reaction may have an initial impact, but then has a longer-term impact such as increased sensitivity to the sun, impacting on lifestyle for a number of years:

> I would say the impact was major. For the period of the reaction I was miserable. I needed to miss work because of it. I felt sick with it as well. So from that point of view that episode was major. It impacted on my holiday. And then I had had subsequent episodes with Ultra violet light exposure, since then. So to me, that's a major impact, because I enjoy the sun, I enjoy being outside, and I enjoy outdoor activities. It means that I have to be extremely careful with exposure to the sun, wear sunscreen, cover up, that sort of thing.

Impact on medical practitioner/consumer relationship

In two of the case studies, the consumers said that although a drug had been associated with a reaction, it did not impact on the medical practitioner/consumer relationship in a negative way. In Julie's case, although she was frustrated by not being able to access information about Tramal and determine the cause of her itching, and would have liked to have been warned that the drug may have particular side effects, it did not appear to affect her trust in her medical practitioners or her decision to trial future medications. James spoke of his suspected ADRs saying that he was not particularly concerned that he had experienced ADRs, and felt that nothing could have been done to prevent them.

Impact on trust

Kay was a person who had experienced uncontrolled epilepsy as a child, but over the past 18 years had lived without experiencing grand mal seizures. The impact related to Kay's confidence, the fear of future episodes of epilepsy, the impact on her family, and the inability to

drive a car. Although the experts and medical practitioners do not believe the epileptic fit experienced by Kay was related to the effectiveness of the generic brand of Epilim, the impact of the episode has decreased Kay's confidence in trialling new medications.

Impact on lifestyle

In Joanna's case, as well as the impact on her physical health, a secondary impact of the suspected ADR was the fact that her holiday was affected, and had to be cut short, and then subsequently, her outdoor recreation had been affected because she is unable to enjoy outdoor activities in the way she used to.

5.2.6.2. The importance of life context

When reading about ADRs in the literature, there is significant emphasis on ADRs that causes death or significant injury. An impact may be significant to the consumer without resulting in an injury that is medically significant. The impact of Edward's ADR was broader than the immediate symptoms of vomiting due to Edward and his wife's disabilities, the fact that Edward was the primary carer for his wife with Alzheimer's disease, and Edward's age. Life context assists in understanding the impact, but it also provides additional forms of understanding.

Julie has a history of chronic pain, Robyn has severe long term uncontrolled epilepsy, and Irene has a history of uncontrolled blood pressure which is complicated further by a significant history of suspected ADRs. In each of these cases, the pre-existing disease is extensive and complex. It is not just a matter of making a diagnosis, and prescribing a drug. In each of these cases, multiple drugs have been trialled over time, and combinations of drugs are juggled in order to maximize the treatment effectiveness. In each of these cases, although ideally the chronic pain, epilepsy and blood pressure would be completely controlled, however due to the complexity of the case, this is unlikely. In each of these cases, therefore, the risk of ADRs is extremely high due to the strength and combinations of medications for Julie and Robyn, and the increased sensitivity to drugs in Irene's case, and so a realistic expectation for these people is to minimize ADRs, but not to eliminate them.

For two consumers, some level of ADR is acceptable. The aim is to maximize the therapeutic benefits, and minimize the reactions, rather than expect to have no reactions. Each time a new

drug is trialled, which may be a new drug on the market, they know that there is a significant chance of a reaction, but are prepared to take the risk in an attempt to manage their condition:

> I suppose I don't see side effects as necessarily being that negative if you can cope with it. I mean I've got tinnitus which they seem to think is from medication and I've got other problems that have come from the medication and that's I mean I have a lot of constipation problems, I've got fatty liver problems, I've got these but I suppose it's weighing up whether it's worth coping. I mean, I mean if it's a side effect it's, I think if it can be handled otherwise I don't necessarily see it as negative because it's just part of it, if you know where it's coming from well that's fine I mean I know when I did go on the Tramal that my ring in my ears got worse and I just said to the doctor just check that there wasn't wax in it and he said no and I thought oh well it must be the tinnitus and that's fine.

One consumer talked about her awareness of the risks and the process she goes through when attempting to decide whether to risk trialling a new medication:

> I was used to the fact that there are new drugs being discovered all the time and he [medical specialist] had told me, and we'd discussed it, that it might have an adverse effect. I read the information that came with the [the drug] because I like to do that. Sometimes I read it for any medication and won't take it after all. I think that maybe I can't stand all those possible side effects. If the information warns about depression I get worried. In fact I've just started a drug called [drug name] which is for severe untreatable acne rosacea. There was a whole book on what would go wrong. In the end I decided to have the [drug name] because the acne was getting quite bad. Yet none of the warnings have happened to me. However, when you're dealing with neurochemistry anything could happen so trying any drug is a bit of a danger.

In contrast, because another consumer has her medication for her epilepsy working extremely effectively, she is not at all prepared to risk changes in medications that may results in an ADR:

> There is some discussion at this point where he [the medical practitioner] wouldn't mind changing me onto another medication, but that's another issue. And I need to decide when and if I want to do that, because I risk, having another one of these [seizures] and not being able to drive, and that's something that I need to do when I haven't got any stresses in my

> life, which I can't imagine that happening (laugh)…….And whilst things are ok, if something's not broke, why fix it. So I'm a bit hesitant there. I think, well this has agreed with me for so long.

In another consumer's case, her history with ADRs in association with anaesthetic drugs has resulted in a significant fear of surgery. The following two consumers are very hesitant to try new drugs due to a fear of something going wrong, a fear based on previous negative experiences associated with drugs:

> I'm terrified of having any more surgery, absolutely terrified. What ever it is, I'll try any other means. I've just had too many bad experiences. In fact I have a problem with my nose where I can't breathe properly, and I've been told I really should have surgery for that, but there's no way I'm having it. I'll put up with anything, I'm just too nervous about surgery now.

One consumer's concern is about working with a new medical practitioner to explain her complex history, and to convince him/her of her history of suspected ADRs:

> Yeah, yeah I do I just hate going to a new doctor because and the older I get the more you forget so if I haven't got it written down, you know, I forget to tell them so yeah I hate it for (laugh) that reason and then to show them all this [past history of ADRs] I hate doing that too (laugh).

For each of these consumers weighing up the risks versus the benefits of taking a medication is based on their life context. The context may include a complex pre-existing disease that has a significant impact on life, and so trialling new drugs is better than living with the pre-existing condition, versus someone with finely balanced medications, where the risk of upsetting the balance is more of a problem than the possible improvement of a new drug. Someone else may have a life where an illness that interrupts that life has a significant impact on people other than the person taking the drug, and for people who have had such negative experiences in the past, it is important to minimize that risk.

Another aspect of life context is that the ADR may have been more or less severe depending on where the consumer was at the time of the suspected ADR. In the case of Helen, the fainting was less severe because she was at home. It could have been significantly more severe if driving a car. This same issue is shared by Kay. If the fit had occurred whilst driving, it would have had a significantly greater impact, than having a fit at home.

These are factors that are essential to consider when assisting a consumer make risk benefit decisions about drugs.

5.2.6.3. Differences between expected versus unexpected symptoms

In a few cases the consumers were accepting of uncomfortable symptoms that they expected but were distressed when they did not know the cause of symptoms. One example was the consumer who suspected Zyban of causing Bell's Palsy. The quote below indicates an acceptance of some symptoms that were severe enough to stay home from work:

> Headaches are one of the side effects of [the drug] as is throwing up…they were enough to prevent me from working, lying in bed in darkness…The doctor said no, no, no that's alright. It's just side effects so I continued.

The following two quotes indicate the stress associated with not knowing the cause of the symptoms of the suspected ADR:

> I think that if I'd known that that was possibly a side effect it would have been less traumatic because it was really quite stressful not knowing why.

> The double vision was distressing, because I'd never had it before, and didn't know why I had it.

The consumers were asked if they would do anything differently or would have liked the medical staff to do anything differently if they were to face the same circumstances again, using the advantage of hindsight. The majority of the participants indicated they would have liked to have been warned that the medication they were taking may result in a reaction. Some also indicated that some idea of when to seek medical advice would have been useful.

5.2.7. SUMMARY OF CONSUMER GROUP ANALYSIS

The consumer group analysis included analysis of the consumer interviews. It provided insight about the decision-makers in the ADR domain, and the decision types made by consumer decision-makers, how consumers use terms such as ADR, side effect and allergy, some problems when making ADR decisions, the resources used by consumers when making ADR decisions, and how ADRs affect consumers and the impact this has on future decision-making. The key results have been summarised below:

- This set of data indicates that consumers are decision-makers in the ADR decision domain, and make a wide variety of decisions including diagnostic decisions, treatment decisions and decisions surrounding information sharing and information seeking.

- ADR decision support includes medical practitioner only decisions. These data suggest that consumers are also actively involved in this decision domain, and play an important role in the detection of ADRs.

- The consumers used the terms 'reaction', 'side effect' and 'allergy'. They appeared to use the term 'side effect' to describe a drug, and 'reaction' to describe a consumer experience. They also appeared to view a 'side effect' as a known and tolerable non-therapeutic effect of a drug. 'Allergy' was used as a type of 'reaction'.

- Issues surrounding the medical practitioner/consumer relationship related to ownership and responsibility issues surrounding health care. The consumers as a whole would have liked to take more responsibility for their health care and the decisions surrounding their treatment.

- The consumers expressed that they would have liked more access to information about prescription drugs and/or the pre-existing condition, to assist in their ability to make informed decisions.

- The consumers made some decisions that may have contributed to the existence of their ADRs including ignoring recommended dosages and choosing not to share particular information with their medical practitioners.

- This set of data highlighted some of the impacts of the suspected ADR other than the immediate impact on the consumer. Other impacts included a continuation of the ADR after the drug had been ceased, the impact on the immediate family, the impact on the medical practitioner/consumer relationship, and on trust and lifestyle.

- When making decisions surrounding prescribing this set of data highlighted a need to consider life context. For some consumers some level of ADR is acceptable due to the complexity of the case and the difficulties surrounding controlling the pre-existing condition, where as for other consumers their medications are finely balanced and so any ADRs may have a negative impact. For some, having had significant negative experiences with drugs, it is important to minimize the risk of future ADRs due to the impact on future decision-making.

- The final result from this group of data was that consumers appeared to be more accepting of non-therapeutic symptoms associated with drugs when they were aware that they may occur, than when they appeared with no apparent cause. This may be another factor to support the argument that providing information to consumers assists in the management of ADRs.

The following section presents the results from the analysis of the medical practitioner data.

5.3. Group analysis - Medical practitioner view

The medical practitioners, who were approached to participate in the study, were asked to discuss the ADR suspected by the consumer by referring to their medical notes, and providing an interpretation as required. As well as discussing the specific ADR in the case study, the medical practitioners were asked some general questions to explore reasoning behind their clinical decisions and to provide some insight into the medical perspective of some issues raised

in the consumer interviews. This section includes the results of the medical practitioner data only.

Seven of the 15 case studies included a medical practitioner perspective, with one case including two medical practitioner perspectives. In total, therefore, this group data includes the views of eight medical practitioners comprising four GPs, three specialists, and one hospital based medical practitioner.

This section, again, follows the general structure of the research questions, followed by the key themes that have emerged from the data analysis.

5.3.1. WHAT DECISIONS ARE MADE BY EACH DECISION-MAKER?

The decisions made by the medical practitioners were identified by the processes of coding described in section 3.5.5.1. Table 5-4 includes a general decision type description in column one, and the decisions made by the medical practitioner group in column two.

The contents of Table 5-4 reinforces the view that decision-making surrounding ADRs is complex, and involves a range of decision types which are more extensive than the medical decisions currently supported in ADR decision support systems.

5.3.2. WHAT DO DECISION-MAKERS UNDERSTAND BY THE TERM ADR?

The medical practitioners used the same set of terms used by the consumers, 'side effect', 'reaction' and 'allergy' to describe symptoms that were associated with drugs. In addition, they also referred to 'significant reactions' and 'significant side effects'. Below are some meanings that have emerged from this set of data.

5.3.2.1. 'Side effects' as an attribute of the drug and a description of the consumer's experience

The consumers referred to side effects as an attribute of the drug as in section 5.2.3.1. The medical practitioners also described side effects as an attribute of the drug. For example, Dr. Price referred to the "…side effects of Zyban…"

Decision Type	Decisions
Prescribing decisions	Decision to use drug therapy
	Determine drug to prescribe
	Determine dosage and duration of drug therapy
	Cease a medication
	Continue with medication, even if reaction present
	If decision to cease medication, decide the time required to cease a medication (slowly decrease one and increase the other; stop one and start another; stop one, wait and then start another.)
Diagnostic decisions	Determine a range of possible diagnoses for symptoms, and to determine the most likely diagnosis/es.
	Determine if one of the possible diagnoses is an ADR
	Determine which symptoms are likely to be associated with which diagnosis
	Whether tests are required to assist with diagnosis
	Which tests to order or conduct
	Determine the severity of the reaction and the likely progression
	Determine whether treatment is required for an ADR
	Whether to consult information to assist with diagnosis, and if so, which source of information
	Determine which pieces of information are relevant and those that are not relevant to the diagnostic decision.
Treatment decisions	Whether to treat the ADR, or allow it to resolve itself.
	Whether to access an external source of information to make treatment decisions (database, text, colleague)
	Determine the amount of investigation to conduct whilst working within ethical limits
	Decide how often the consumer needs to be monitored, and the frequency of monitoring
Reporting decisions	Whether to report a suspected ADR to ADRAC
	Which information to report
Seeking information	Determine when to seek further information and who to seek it from (such as consumer, text book, colleague, database, pharmacist)
	Determine which information to seek from each source
Sharing information	Determine the information to share with the consumer, and the level of information to share.
	Determine a method of conveying information to consumers to avoid information overload, but provide information requested and required by consumers.

Table 5-4 Decision types made by medical practitioners

The medical practitioners also referred to 'side effects' as symptoms experienced by the consumer. One medical practitioner used the following phrase. "I just think that she was certainly having side effects of [the drug]."

5.3.2.2. 'Side effects' as unwanted, known or expected, non-therapeutic effects of medications

In addition to the terms as attributes of drugs and or consumers, most of the medical practitioners used the term 'side effect' to describe non-therapeutic effects of a drug, that have a known set of attributes such as a set of symptoms, the consumer group likely to experience ADRs, and an expected time frame. Some examples are listed below:

> It's unusual in the post menopausal women to have these side effects. It's usually with younger women that are pre-menopausal.

> Side effects of [the drug] are usually on mental function rather than nerve function.

> [I] did the liver tests to check for hepatitis, which is a possible side effect of the group of drugs, know as statins.

> My only experience with all that is that when women usually get with those sort of things, they get it earlier on, they don't get it two years after starting tamoxifen…

> …sometimes what I do is print out a list of known side effects of medications.

The above examples use the term 'side effect' as a set of symptoms known to be related to a drug. Dr James, however, used the term 'side effect' to describe symptoms associated with the drug that are not well known. He was talking about when ADRs should be reported to ADRAC. "I just stop the drug and change things around, but if it's a side effect of the drug, which is uncommon, or it may not have been described, well you should report those."

5.3.2.3. 'Significant side effects'

Several medical practitioners referred to 'significant' side effects. The implication appears to be that a significant 'side effect' may be one that has an impact on the consumer, as opposed to insignificant side effects which can be tolerated, or which will not prevent the consumer from continuing to take the medication. One medical practitioner used the term as follows. "…she

started off on the [the drug] and she didn't have any significant side effects for the first six to eight months."

5.3.2.4. Differences between the terms 'side effect' and 'reaction'

Some of the medical practitioners made a clear distinction between the term 'side effect' and 'reaction'.

> I'm not sure if there was a reaction, but I just think that she was certainly having side-effects of [the drug]. And it's well recognised that a proportion of patients just can't tolerate [the drug].

5.3.2.5. 'Reaction' as an attribute of the drugs and description of the consumer's experience

Although some medical practitioners distinguished between 'side effects' and 'reactions', they appear to have been used in a similar way. Like the term 'side effect', 'reaction' was used as an attribute of the drug, such as "…it's a known medication to have potentially significant reactions". It was also used as a description of the consumer's experience such as "…she has had adverse drug reactions to [reading a list of drug names] …"

One medical practitioner said that he sees 'side effects' and 'reactions' as different terms to refer to the same concept.

5.3.2.6. 'Significant reaction'

The term 'significant' was also used with the term 'reaction', for example "even though it was a quite significant reaction, I think it responded reasonably quickly."

Another similarity between the term 'side effect' and the term 'reaction' was that reactions were also used to describe non-therapeutic symptoms that were associated with a drug, which had particular characteristics. Some examples are below:

> [The medical practitioner] said that normally a reaction to a medication would cause pain on both sides of the body and be constant pain, where as [the consumer] experienced the pain only on the right side, and the pain was worse with specific activities such as driving.
>
> [The medical practitioner] said he has seen reactions to [drug class] in the past, and the person usually has pain down both of the large muscle groups in the legs often unable to stand up.
>
> I don't think there is evidence that [this drug] causes this sort of reaction.

Although the terms 'side effect' and 'reaction' have been described as being different terms, they appear to be used the in same way, and have the same characteristics. The only difference may be severity, with 'reactions' as more severe than 'side effects', however as the term 'significant' was used with both terms, it appears that there can be more severe and less severe 'side effects' and 'reactions'.

There are not enough examples within these data to determine if the terms are used to mean similar concepts, or whether different medical practitioners have different understandings and uses of the term.

5.3.2.7. Allergies

The term 'allergy' was only used by three of the medical practitioners and appeared to refer to a specific type of reaction. Of the case studies with a medical view, there were only two that were described by the medical practitioners and experts as being classified as an 'allergy'.

The term 'allergy' is defined in the Medline Plus online encyclopaedia as follows:

> Allergy is caused by an oversensitive immune system, which leads to a misdirected immune response. The immune system normally protects the body against harmful substances, such as bacteria and viruses. In contrast, an allergic reaction is when the immune system reacts to substances (allergens) that are generally harmless and in most people do not cause an immune response (Medlineplus).

This term appeared to be consistent with how it was used by these medical practitioners. In most cases the medical practitioners referred to drug allergies, but Dr Carey also referred to Joanna's allergy to nuts.

One medical practitioner referred to the diagnosis of an allergic reaction, as having particular characteristics that can be recognised:

> It looked like an allergy. She had inflamed eyes on that day as well. It just looked like an allergic reaction. Particularly two days later when she had the rash, it was definitely an allergy, but even on the first presentation, it looked like an allergy.

5.3.2.8. Misunderstandings related to terminology

One medical practitioner referred to confusion in the terminology between medical practitioners and consumers. He was referring to consumers who come to the medical practitioner with a suspected 'allergy' to a drug:

> …most of those are not allergies, they're nausea, and some tummy upset, that's quite possible without an allergy, but it's difficult to know, sometimes if they are truly allergic, or whether they're getting some significant side-effects, or whether it's, having read it, it's the way they believe it's gone, or whatever. It's hard to tell.

Interestingly, it appears that the consumers referred to by this medical practitioner are using the term 'allergic' as a general term to mean 'symptoms associated with the drug', and he understands them to literally mean an allergy, rather than using the term 'allergy' to mean the more generic terms of 'reaction' or 'side effect'.

The statement quoted by one medical practitioner earlier, "I'm not sure if there was a reaction, but I just think that she was certainly having side-effects of [drug name]," may indicate that the medical practitioner was using the term 'reaction' to mean 'allergic reaction' and again, the symptoms suspected by Mary were not 'allergic' in nature, but she did feel may have been associated with the medication.

This section indicates that there appears to be some confusion in the terminology. In some cases, the terms 'side effect' and 'reaction' appear to be largely interchangeable, with the term 'allergy' referring specifically to an immunological response.

In chapter six, the use of these terms will be discussed to determine if there is an impact of different groups using terminology differently, as it relates to the detection and management of ADRs, and implications for decision support.

5.3.3. HOW ARE ADR DECISIONS MADE?

The primary decision type described by the medical practitioners during their interviews was the differential diagnosis between one or more suspected conditions. A condition may include the pre-existing disease, and newly developing disease, an ADR or a combination of these.

5.3.3.1. Differential Diagnosis

The analysis of the medical practitioner data revealed some strategies medical practitioners used when attempting to differentially diagnose an ADR. The strategies discussed in this section include novel decision-making and the use of negative knowledge, pattern matching, and the differences between specialists and GPs.

Novel decision-making and lack of knowledge

In some of the case studies, the medical practitioner indicated that he[6] had little or no experience with a suspected ADR by either stating it directly, or by seeking advice from colleagues or information sources, appeared to have little or no previous experience.

As an example, one medical practitioner stated that he had not seen photosensitivity linked to NSAIDs:

[6] When referring to the group of medical practitioners, rather than using the term s/he as previously used in this document, as all medical practitioners are male in this study, the term he will be used.

> I've seen photosensitivity reactions to things like tetracyclines. I certainly haven't seen it to an NSAID. I've seen it with St John's wort. The short answer is, no, I haven't seen it to that group of medications. In my experience, this is not a common problem.

In two cases, the consumer indicated that the medical practitioner sought advice from either a colleague or a database, indicating it was a novel diagnosis, not one that was immediately recognised by the medical practitioner.

One of the strategies that appeared to be used when making a novel decision was the use of a process of elimination. One medical practitioner described this process:

> Her regular routine hadn't altered, and so, because that is a known side effect and she consulted the literature herself, you know, being in the medical field she'd gone straight to the literature, she'd made that diagnosis and conclusion herself. I was happy to go along with that. That seemed reasonable…It was a severe photosensitivity reaction, so it wasn't as if it was a rash, a mild rash by a viral illness, or a brief rash you might get for a week or two that would occur perhaps after an anti-biotic. She hadn't been unwell in any other way. That was the only change to the routine, so it's highly probably that that was the cause of the problem.

Pattern matching

In some of the other cases, when asked if the medical practitioner used an external source of information to assist in the diagnostic process, he stated that he was very familiar with the ADR due to years of medical experience. One medical practitioner said "I know about [the reaction] because I've seen it. I've experienced it." Another one stated, "[I have] a lot of experience with these drugs, I've had many years of experience, most of my patients are on [this drug]."

One medical practitioner used pattern matching, also as a method of eliminating possible diagnoses. "My only experience with [this drug] is that when women usually get with those sort of things [symptoms described by consumer], they get it earlier on, they don't get it two years after starting [the drug], you know".

One medical practitioner also began with a familiar diagnosis, but there was a variation of the details of the diagnosis for this specific consumer. In this case the medical practitioner said that he was familiar with the suspected, reaction, however not at the dose the consumer was taking. "In my experience most people who got drug induced lupus from [drug name] were taking 200mg three or four times a day, not 50mg twice a day which is what [the consumer] was taking."

5.3.3.2. Differences between GPs and specialists

The use of pattern matching for ADRs was stronger from the group of medical specialists, compared with the GPs. Each of the specialists interviewed, when asked if they accessed additional resources to assist with their decision-making, said that they were very familiar with the drug and class of drugs in question. Of the GPs, however, there was only one that indicated the diagnosis was made through recognition, "it looked like an allergy". Each of the others described a diagnostic process of considering multiple options, and weighing up the likelihood of each option.

The analysis of the medical practitioner data has provided some insights into methods used by the GPs and specialists when attempting to differentially diagnose between an ADR and a disease. Nine clinicians provided some insight, however when attempting to look at the differences between GPs and specialists, the groups contained only four cases, making it difficult to do more than suggest these processes be explored further in future research.

5.3.4. WHAT PROBLEMS OCCUR WHEN MAKING ADR DECISIONS?

The medical practitioner data provided some insights into some of the problems surrounding ADR decisions. This section discusses the information needs of consumers, and the concerns of medical practitioners surrounding information, and the use of the term 'compliance' and the implications of this term in this decision domain.

5.3.4.1. Information required by consumers

The analysis of the consumer data highlighted the issue that consumers would like more information about potential ADRs associated with prescribed medications. This issue was discussed with the medical practitioners, and the following concerns emerged.

Medical practitioners view of providing ADR information to consumers

Several of the medical practitioners interviewed discussed a concern about providing ADR information to consumers. One medical practitioner articulated this concern below:

> Information is given. They go to a chemist. The pharmacist gives them an enclosed brochure. Now for some people that's just terrific, and for some people it's a disaster.

The medical practitioner's expressed a belief that some consumers will over estimate the risk of taking a medication, compared with the risk to their health of not taking the medication or not treating the underlying condition. The concerns appeared to fall into two categories; those related to a consumer choosing not to take a medication, and concern that providing information will result in a nocebo effect. These are discussed below.

Consumers choosing not to take a medication

Two of the medical practitioners spoke of their concerns surrounding consumers choosing not to take medications when provided with detailed ADR information:

> They just, every symptom they believe will potentially happen to them, and some of these things, in the ultimate, they can be very very nasty reactions. The one I was talking about with the hepatitis, that person was really quite sick, but it's one in whatever it is rare, and but people, some people don't like taking medication say, right well I'm not taking the medication, when they truly need the medication. That sort of person is not getting the benefit you thought might be worthwhile…The old power of suggestion is pretty strong. And if you're wanting someone to really take a medication for some serious problems and they don't then you've lost the opportunity you had.

> I think it depends on the particular individual. For some people, knowledge is power, and for some people knowledge is destructive, and unfortunately there are a group of people in whom, if you provide them with the prescribing information and the side effect profile of a medication, they'll flatly refuse to take it, even though the chances of them having those side effects are miniscule, simply because the drugs sound far too dangerous. On the other hand there are a group of people who, when they have that information, they just say, that's ok,

> that's interesting, I'll see what happens. You can't predict which way people are going to respond.

According to one medical practitioner, the product information provides the reader with information about the types of symptoms that may be associated with the drug, but not a clear indication of the likelihood. He also stated that the risk of taking the drug needs to be weighed against the risk of not taking the drug, something he feels the consumer does not do, if provided with the information about possible reactions.

The nocebo effect

The second concern raised by the medical practitioners was that information may result in the consumer experiencing a nocebo effect.

The nocebo effect was described in the literature review (chapter two). The nocebo effect is when a consumer takes a substance that does not cause harm, such as a sugar tablet, but when the consumer believes it may cause harm, s/he experience harmful effects, which are perceived to be due to the drug. It is a concept described also as a negative placebo effect.

Some of the medical practitioners indicated the difficulty in differentially diagnosing a reaction to a medication versus a nocebo effect:

> I'm just thinking about one person…they imagine every side effect possible…They are not all realistic side effects…it's difficult to know, sometimes if they are truly allergic, or whether they're getting some significant side-effects, or whether it's, having read it, it's the way they believe it's gone, or whatever. It's hard to tell… The old power of suggestion is pretty strong .

The medical practitioners did not offer a solution about how to make this differential diagnosis, apart from being aware that it can happen, and to limit the level of detailed information provided to consumers.

Using information to support medical reasoning

One medical practitioner said that he uses information to reassure consumers that a medication is not associated with a drug, when they have heard from friends and/or family that:

> …sometimes what I do is print out a list of known side effects medications. It's mainly just to reassure them, it's not related to a drug but sometimes they get a bee in their bonnet that they don't want to take a drug, because they had one of their friends on it, and it wasn't good, you know, caused something terrible, and you know and then they want to get off it.

5.3.4.2. Medical practitioner/consumer relationship

Many issues related to the medical practitioner/consumer relationship were highlighted in either the individual case study analysis, or the analysis of the consumer only data. One issue related to the use of language raised in the medical practitioner data, was the issue of 'compliance', and the problems perceived by medical practitioners when consumers are 'non-compliant' surrounding prescription medications.

Compliance

Compliance and non-compliance were terms used by the medical practitioners, but were not found in the consumer interviews. The term non-compliance appears to imply that the medical practitioner has made a recommendation for a drug therapy, and the consumer has either not taken the drug/s, or has not taken the drug/s using the recommended instructions (time of day, dosage). The previous section showed that medical practitioner's were concerned that providing detailed ADR information may cause non-compliance, that is, a consumer choosing not to take a medication recommended by the medical practitioner, for a reason the medical practitioner considered is based on misunderstanding information. The text below describes one medical practitioner's concerns over non-compliance:

> And the other one [issue] is just ordinary compliance. People saying they'll do it, but they don't do it, either by forgetfulness or deliberately not wanting to take it, and you think they are taking it.

> I don't know how to get over the compliance factor apart from talking to people and hopefully they see it as being important…you don't know whether to increase medications.

> You assume things are being done…So you're not sure whether the medication's not working, or whether the medications not being taken.

An additional issue highlighted by one medical practitioner above, is the lack of honest communication between the medical practitioner and the consumer. He expressed frustration in attempting to determine if a drug is working or not, as he is not sure if the consumer has taken the drug or not.

Compliance will be discussed further when examining medical practitioner/consumer decision models in section 6.3.2.

5.3.4.3. Complexities of diagnosis

The medical practitioner data highlighted two factors that add to the complexity of ADR diagnosis, whether a medication is essential or non-essential, and the factor that diagnosis is an inexact science.

Essential versus non-essential medications

Managing an ADR from a non-essential drug appeared to be less complex than when managing a drug that is essential.

One medical practitioner suggested that consumer's decision to cease the drug was a much simpler decision because the medication was non-essential. This contrasts with the decision made by another medical practitioner, who felt the drug could be a very important medication for this consumer, and so the decision to cease the medication was a much more difficult decision given her complex history.

The likelihood that a drug is associated with a medication

As discussed in chapter two, the results of the diagnostic process usually include a likelihood that a drug is associated with a set of symptoms. Causation is rarely stated. The experts classified the ADR according to either, a percentage likelihood, or a level of certainty. Two medical practitioners, below, talk about cases when they do not believe diagnosis is possible, and provide their reasoning.

The first medical practitioner stated that he didn't believe he could make a diagnosis, and that any attempt to do so would be supposition. He said that when there are confounding factors, a diagnosis is not possible:

> I don't think you can, that's the problem. I don't think you can decide. We just know the facts that she had the sleep deprivation, she changed brands and then she had a fit. So putting them all together is supposition. And sometimes, there is more than one factor, and sometimes, a little bit in the presence of the other thing can go a long way, so that if she hadn't had the sleep deprivation, maybe the drug change would not have made a difference.

The second medical practitioner referred to another situation where diagnosis was not seen as possible:

> In a totally separate situation I have a patient at the moment, that is convinced, or the family are convinced that some inhaled medication caused a coma. Now, I can find no reference to that anywhere in the world literature. They could still be right. I mean, she might be the only case where it has ever happened. So you just can't be absolutely certain, but you can only base what you do on the information that's available.

5.3.5. WHAT RESOURCES ARE USED BY DECISION-MAKERS?

The information and knowledge sources used by the medical practitioners when making decisions surrounding ADRs were extracted from the interviews during the coding process. Below are three lists, one of information sources used, the second of knowledge sources used and finally, the content of the information sources used by the medical practitioners.

The same definitions for knowledge and information are used in this section, as in the section describing the resources and information used by consumers.

The sources of **information** used by the medical practitioners included:

- test results (allergy testing, liver function, blood serum, patterns in anti-nuclear antibodies);

- drug companies;
- ADRAC;
- desk top prescribing software;
- databases of medical information (natural health program and the Cochrane Library);
- drug product information;
- opinions of other professionals including:
    - Pharmacists;
    - referrals to medical specialists;
    - consultation with colleagues.
- reference books including:
    - Mims (drug product information);
    - a reference book describing drug levels (when a drug will peak in the blood serum).
- consumer and/or the consumer's family;
- the consumer's medical history.

Sources of **knowledge** used by the medical practitioners included:

- medical knowledge of diseases such as:
    - symptoms known to be associated with particular diseases;
    - typical progression of a disease.
- knowledge of drugs and drug behaviour including the temporal relationships between drug and onset of symptoms;
- knowledge of ADRs (theoretical and from experience);
- knowledge of consumer (from time spent interacting with a single consumer and many consumer's over time);
- observation of symptoms when commencing drug, and when ceasing drug;
- knowledge from experience as a medical practitioner with other consumers;

Content of information and knowledge used by the medical practitioners

- about the consumer included:

  - results of tests (blood serum levels, liver enzymes, allergy);
  - level of drug in consumer's blood serum at a particular point in time;
  - medical history that was:
    - stored by their own clinic or hospital;
    - reported by another medical practitioner;
    - reported by the consumer, including a history of ADRs.
  - dates and times drugs were given and symptoms appeared;
  - individual characteristics of a particular consumer;
  - information about events surrounding commencement of symptoms conveyed by the consumer and/or consumer's family;
  - likely problems associated with particular groups of consumers (eg with a particular condition such as pregnancy or diabetes);
  - consumer preferences for particular treatment options.
- about drugs included:
  - ADRs known by drug companies or ADRAC;
  - ADRs documented in drug product information;
  - therapeutic levels of drugs;
  - prescription, over the counter and complementary medicines.
- about ADRs included:
  - known 'reactions' associated with particular drugs.
- about diseases included:
  - possible diagnoses for a set of symptoms;
  - possible tests available, what they will show and the time taken to receive the results;
  - factors that differentially diagnose two possible diseases.

The sources of information available were not always complete sources of information, because either one party did not share all available or relevant information, or did not have the time/take the time to access the available information. This issue is discussed further in the analysis of the individual case studies in the previous chapter, and again in the discussion of the results in the following chapter.

5.3.6. HOW DO DECISION-MAKERS CONTRIBUTE TO THE CREATION OF NEW ADR KNOWLEDGE?

New drugs are constantly appearing on the market. Each new drug has the potential to individually contribute to ADRs, and also to interact with other drugs currently available. As explained when reviewing the literature in chapter two, before a new drug is released on the market, drug trials are done to determine the safety of the drug, and identify any common and rare ADRs. Because this trial is done with a subset of the community, at the time the drug is released onto the market, all the likely ADRs from the drug are not known. Drug surveillance programs, therefore, are in place to detect and then document additional ADRs associated in particular with new drugs on the market, and to detect any changes in drugs which may be related to the manufacture of the drug, or due to an interaction with a new drug.

The medical practitioners were each asked if they reported the suspected ADR to ADRAC, and to provide a reason for their response.

5.3.6.1. Reporting suspected ADRs to ADRAC

Table 5-5 lists the case studies which include a medical practitioner perspective. Two medical practitioners were involved in Kay's case. Of the nine medical practitioners who participated in the study and treated eight consumers with suspected ADRs, none of them reported the suspected ADR. For three of the consumers, the medical practitioners did not believe the suspected ADR was likely to be an ADR and so did not report it. For the remaining five consumers, three medical practitioners indicated that the ADR was well documented and well understood, and of the five, three indicated that the process of reporting to ADRAC is very time consuming and so they would only be likely to report when a suspected ADR had not previously been documented and/or is not well known, or in serious circumstances.

The reasons the medical practitioners gave for not reporting have been discussed in detail below.

5.3.6.2. Reasons for low levels of reporting

The medical practitioners provided three key reasons for not reporting; the reporting processes are complex, the medical practitioner did not believe there is a high likelihood that the

symptoms were associated with the drug, and the suspected ADR has been previously documented and is well understood.

Complexities of reporting

Three medical practitioners expressed that in the past, they have reported suspected ADRs, and although the actual reporting process was not time consuming, it was the level of detail required

Case Code	Medical practitioner	Report to ADRAC?	Reason
Toni C02	C02GP1 Dr Barns	No	Not the prescribing medical practitioner. Thought the prescribing Dr may have reported it. Also negative past experience with reporting.
Kay C05	C05SP1 Dr Green	No	Unlikely to be an ADR, confounding issues
	C05H1 Dr Nash	No	Unlikely to be an ADR
Helen C06	C06H1 Dr Stevens	Not asked	Dr Stevens indicated that this reaction is very common.
Mary C07	C07SP1 Dr O'Neil	Not asked	Unlikely to be an ADR
Tim C09	C09GP1 Dr Price	No	Unlikely to be an ADR
Irene C11	C11SP1 Dr James	No	ADR previously well described and understood (although not at the dosage taken by this consumer)
Joanna C13	C13GP1 Dr Carey	No	Probably should have reported it. Didn't due to being busy and focus on consumer management.
Paul C17	C17GP1 Dr Lang	No	ADR previously well described and understood. ADRAC processes too time consuming to report well documented ADRs

Table 5-5 Reporting of suspected ADRs to ADRAC

when staff from ADRAC followed up the suspected ADR that was the concern. Two examples follow:

> Well, I reported one. I can remember one case I reported of a serious reaction. And it had to be reported, it should have been reported, it needed to be reported, but the amount of

> detail that they wanted, it made it, you thought, gee you wouldn't do this unless you really had to do it, unless it was very important, because you couldn't answer some of it. You didn't know some of it, so much detail. Sure necessary detail but some of it, it would be nice to have it all, but sometimes you just haven't got that. All we are saying is look I think this is a serious reaction, it was hepatitis that developed from this, but I don't know why, you know, they wanted to know this and that, liver biopsy, no I haven't done a liver biopsy. I'm telling you about this, if you want to know any more, you follow it up, so it was a little bit demanding [laugh]. I do it for serious things. It really has to be a serious reaction.

> I mean, certainly I have reported things in the past, and essentially it's, well, it's a bit of a rigmarole…The rigmarole tends to be, not the initial reporting of it, but then the follow up. Often they will come back with follow up questions, and then you have really got to go through even more of the history and all the rest of it, which I understand from their point of view is part of the process, but yes, it's not so much just the initial filling in the blue form and sending it away.

Unlikely to be an ADR

The second reason given for not reporting an ADR was that the medical practitioner believed the symptoms were more likely to be associated with another condition, than with the suspected drug. One medical practitioner commented that if he had been certain that the symptoms were associated with the suspected ADR, he would have reported it, however because there were confounding factors that may have contributed to the incident, the decision was not to report.

> Oh no, I think if I had believed it, you know, I would have reported it. I believe there was a definite reaction. I must say, I tend not to report things that I think are confounded. If she hadn't had the sleep deprivation and had had it, I'd definitely report it; but no, not with the other things. This was also complicated by me not seeing her at the time. I saw her, a couple of months later.

ADR previously documented and well understood

A final reason the medical practitioners said they did not report the suspected ADR, was because it had already previously been well documented and described.

> I would normally report unusual reactions. I wouldn't normally report reactions which have previously been well described, and therefore, I don't think need to be. For instance, this is a recognised situation. If someone is on lipid lowering therapy and they develop myositis, muscle aches and pains and their CPK level goes up, it's a recognised complication of [the drug], so do you notify? Well I don't, I just stop the drug and change things around, but if it's a side effect of the drug, which is uncommon, or it may not have been described, well you should report those. That way a database is built up.

The medical practitioners each provided one of the above reasons for not reporting the suspected ADR. The next section discusses some implications for this lack of reporting.

5.3.6.3. Concerns about a lack of reporting

In this study, none of medical practitioners reported suspected ADRs for a variety of reasons. As discussed when describing the processes surrounding ADR reporting, a key method in detecting ADRs associated with a drug that were not detected in the initial drug trials, is through voluntary reporting processes. If the following ADRs that were not reported had been reported by either, the medical practitioner, the prescribing clinician or the consumer, the following contributions would have been made to new knowledge:

- Hydralazine: The link between hydralazine and lupus has been well documented, but not at the dosage taken by the consumer.
- Zyban: The results of this case study suggest it is unlikely there is an association between Zyban and Bell's Palsy. Zyban, however, was a new drug on the market, and Bell's Palsy may have been a rare ADR associated with Zyban not yet recognized and documented. One method this association would be made is if cases from around Australia and the World were reported, which would result in a signal in the ADRAC database. If, because it is unlikely, it is not reported, new signals cannot be generated.

The following reactions, due to their severity, if reported, would assist ADRAC in monitoring the occurrence of severe reactions, and monitoring the extent to which prescribers use 'known' information when prescribing. As well as documenting new ADRs that have not previously

been described, ADRAC at times notices reports of drugs that have been described, and include a reminder to ADR decision-makers:

- Tegretol was associated with a severe reaction that looked like flu symptoms. Has been previously documented, but the medical practitioner did not recognise it. Reporting may have prompted ADRAC to publish a reminder in *The Australian Adverse Drug Reaction Bulletin*.
- Celebrex was associated with a severe photosensitivity reaction that has had an impact on the consumer for the past two years was not reported. Although the association between Celebrex and photosensitivity reactions is documented in the product information, the medical practitioner was not aware of this association. Again, this may have indicated to ADRAC that a reminder may be useful.

5.3.7. SUMMARY OF THE MEDICAL PRACTITIONER GROUP ANALYSIS

The medical practitioner data comprised four GPs, four specialists and one hospital medical practitioner. The nine medical practitioners were the medical practitioners for eight cases, as one case study includes two medical views. Below is a summary of the results from this section:

- The data suggest that medical practitioners are involved in decision types broader than those currently supported by ADR decision support. The decision types included diagnostic decisions, prescribing decisions, treating decisions, decisions surrounding ADR reporting, information sharing and information seeking.

- The terms 'side effect', 'reaction' and 'allergy' were used by the medical practitioners. Although they indicated that there is a difference between 'side effect' and 'reaction', the uses of the terms were similar. 'Allergy' was used as a subtype of 'reaction'. These data also implied that differences in terminology between medical practitioners and consumers may result in misunderstandings between decision-makers.

- This set of data highlighted some methods used by the medical practitioners when attempting to differentially diagnose between ADRs and other conditions. In some cases,

the medical practitioners made novel decisions having never seen the symptoms associated with a drug in the past, and in other cases they appeared to have used a pattern matching approach when making familiar diagnostic decisions. The specialists in the study all used a pattern matching diagnostic style, and most of the GPs used diagnostic processes associated with novel decision-making.

- The medical practitioners were concerned that providing detailed ADR information to consumers may result in them either choosing not to take an essential medication due to their inability to weigh up the risks of taking a medication compared with the risks of not treating a disease. They were also concerned that the detailed information may result in some consumers experiencing a 'nocebo', or negative placebo effect.

- The term 'compliance' was used by medical practitioners, but was not a term used by the consumers. Two issues associated with compliance and ADRs raised by the medical practitioners were that detailed ADR information may be associated with 'non-compliance', and 'non-compliance' makes it difficult for medical practitioners to determine if the drug therapy is not working or if the consumer is not taking the medication.

- Two complexities in the diagnostic process raised were the issues of essential versus non-essential medications, and difficulties of making inexact diagnoses, and in some cases diagnoses were not seen as possible.

- The final result from this section were issues surrounding reporting of ADRs to ADRAC. In this study, none of the suspected ADRs were reported to ADRAC. Three reasons were provided by the medical practitioners; the reporting processes are complex and time consuming, that the medical practitioner did not believe the symptoms experienced by the consumer were likely to be a suspected ADR, and finally that the ADR was well documented in the literature and well understood.

5.4. Group analysis – expert view

The expert views alone, provided significantly less insight when analysed as a group, than when analysed at a case level. The key results from this chapter include insight into the definitions

used by ADRAC, and some factors the experts believe may have assisted in the prevention, early detection and/or management of ADRs.

5.4.1. WHAT DO DECISION-MAKERS BELIEVE IS AN ADR?

ADR definitions were discussed when reviewing the literature (section 2.2.1). The experts use the World Health Organization (WHO) definitions. According to WHO, the term 'unexpected' has been included to indicate the subset of ADRs of most interest to drug surveillance programs.

Side effect

> Any unintended effect of a pharmaceutical product occurring at doses normally used in man which is related to the pharmacological properties of the drug (WHO, 2004).

According to WHO the term 'side effect' is an old term that includes positive and negative unexpected effects. It is used synonymously with the term 'ADR', but is less specific. They recommend the term ADR is used instead as it is more specific.

A discussion with one of the experts about the differences between an 'ADR', a 'side effect' and an 'allergy' revealed the understanding that an allergy is a subset of an ADR. One complexity discussed was that the expert's perspective was that a consumer may use the term 'allergy', when meaning an 'ADR', but a medical practitioner may hear 'allergy' and not understand that the consumer really means the generic form of an 'ADR'.

The expert said that he believes people may use the term 'side effects' to describe common ADRs that are generally well understood and well documented. He said he believes that Type A reactions, which are dose related, are commonly referred to as side effects.

5.4.2. FACTORS THAT WOULD ASSIST IN THE PREVENTION, DETECTION OR MANAGEMENT OF ADRS

Table 5-6 lists each of the case studies, and summarises whether the experts believe the suspected ADR fits the WHO definition of an ADR, whether prevention was possible and whether earlier detection was possible. Reasoning and complexities have also been included in

this table. In most cases, using the advantage of hindsight, the experts believe that something could have been done to either prevent or detect each of these suspected ADRs earlier.

5.4.3. SUMMARY OF THE EXPERT GROUP ANALYSIS

The analysis of the expert questionnaires provided results that relate to the use of terminology surrounding ADRs, factors that occurred in the case studies that may have resulted in a preventable ADR, or delayed detection of an ADR, and the complexities that make ADR diagnosis difficult.

The experts had the advantages of hindsight, and of viewing both the consumer and medical data for a case. Neither the consumers nor the medical practitioners had access to all of the information. The results from this section, therefore, cannot reasonably state what each party should have done, all they can suggest is that certain behaviours may have contributed to the occurrence of, or delayed detection of an ADR, but with the acknowledgement that the decision-makers at the time did not have access to the information available to the experts.

The experts used the WHO definitions for 'reaction' and 'side effect', which have been re-iterated in this section. Implications of each participant group using these terms differently will be discussed in the following chapter.

The expert data provided insight into factors that may have prevented or detected suspected ADRs in these case studies. The factors can be summarised as follows:

- Awareness of drugs which are contraindicated for particular groups of consumers.
- Awareness by the consumer and/or medical practitioner that a possible diagnosis for a set of newly presenting symptoms is an ADR.
- Providing consumers with warnings about suspected ADRs and/or written information about known risks of medications.

5.5. Combined methods case study analysis

There are several results which were not able to be satisfactorily presented by either viewing them at the case study level, or at the group level. When they were discussed using the group and individual case study results together, they provided a meaningful result. The two sets of results in this section include a discussion of how consumers contribute to diagnostic decision-making, and medical practitioner/consumer decision-making models.

5.5.1. HOW ARE ADR DECISIONS MADE?

Understanding how ADR decisions are currently made can assist in understanding why ADRs continue to occur, and determining gaps that, if filled, may assist in the prevention, detection or management of ADRs. The consumer interviews provided insight into the information and knowledge sources used in order to make their ADR decisions, and also some understanding of the difference between traditional medical diagnostic decision-making, and ADR diagnostic decision-making. This consumer group information, however, is more meaningful when in the context of the expert and medical practitioners is included, and it is therefore included in this section of analysis.

5.5.1.1. Differential diagnosis - Consumers

Past literature supports the notion that consumers are becoming more involved in medical treatment decisions (as discussed in chapter two) however diagnostic medical decision-making, is generally considered a task for medically trained personnel. Some of the consumers in this study, believe they have been involved in diagnostic decision-making, as previously discussed. It is interesting to consider, therefore, whether diagnostic decision-making in the area of ADRs is different to traditional diagnostic decision-making.

Table 5-7, includes the consumers who believe that s/he was the person who initially suspected that the drug was associated with the symptoms. In each of the cases, two experts provided an opinion about whether they believe the symptoms were associated with the suspected drug. In several of these interviews, the consumer described the reasoning behind their suspicion.

	ADR?			Prevention?			Earlier detection?			Suggestions to prevent or detect ADR earlier	Complexities in each case
	E1	E2	E3	E1	E2	E3	E1	E2	E3		
Toni C02	Y	N		N	N		Y	N		If consumer had sought advice earlier. If consumer had been warned that a "flu like virus" can be an ADR. If medical practitioner had recognised possible ADR earlier and done tests to support this.	Symptoms of suspected ADR very similar to symptoms of influenza virus. Possible that consumer had virus AND ADR.
Julie C04	Y	Y								Perhaps treat pruritis with a different anti-histamine Provide consumer with ADR information	Chronic pain very difficult to manage Often can't avoid ADRs
Kay C05	N	N									General suggestions for prevention of epilepsy included avoidance of alcohol, and sleep deprivation.
Helen C06	Y	Y		Y	Y		N	N		Not to take drug prescribed for someone else	
Mary C07	N		Y			N			Y	Earlier consideration that the symptoms may have been caused by the tamoxifen	Another possible diagnosis that also fits the symptoms
Belinda C08	Y	Y		Not sure	N		Not sure	Y		Medical staff could be more aware of possible complications with Beta Blockers	Likely to be an interaction, but unsure of which drugs were interacting due to lack of medical information
Tim C09	N	N									Difficult to determine the effects of the nicotine withdrawal compared with the effects of the Zyban.
Edward C10	Y	Y		Y	N		N	N		Vomiting could have been treated Possible hospitalisation for consumer of this age. Second ADR could have been avoided with recognition of first ADR.	Second bout of vomiting significantly more severe that would be expected from ADR alone. Suspect another complication.
Irene	Y	Y		N	N		Y	Y		ADR well documented and	Very generalised symptoms may have

C11										understood Consumer history of ADRs known to be "sensitive to many drugs". Earlier testing for lupus or cessation of drug.	made detection complex
James C12	Y	Y		N	N		N	N		Multiple instances of the reaction assisted with detection	
Joanna C13	Y	Y		Y	Y		Y	N		NSAIDs should be avoided with Joanna's history of anaphylactic reaction to nuts. Used physical therapies rather than drug therapies Seek medical assistance earlier	
Bob C14	Y	N		N			N				
Kerry C15	Y	Y		N	N		N	N			This experience has reinforced her fear of surgery and anaesthesia which may have the effect of further limiting future therapeutic options.
Robyn C16	Y		Y	N		N	N		N		"…the specialist was kept appraised but elected to continue this therapy notwithstanding the symptoms reported by the patient." This was because he believed this medication may be useful once ADR settled.
Paul C17	Y	Y		N	N		Y	Y		"…if the patient had been better warned, the association would have been more quickly recognised and management (by stopping the drug) would have occurred much more quickly." Better communication between medical practitioner and consumer.	The symptoms were general, and could have been attributed to a number of factors. Significant difference between the consumer's perception of the severity and the medical practitioner's.

Table 5-6 Expert opinion on the prevention and detection of suspected ADRs

Paul and Joanna both have backgrounds in a medically related field and so will not be included in this section, as the aim is to understand about how diagnostic decisions have been made by non-medical personnel in the area of ADRs. The remaining consumers in Table 5-7, suspected a relationship between the drug and symptoms without medical training.

Temporal relationship between drug onset and symptoms

In six of the eight cases in Table 5-7 there was a clear relationship between the time the consumer took the drug and the onset of the symptoms.

Tim had headaches and vomiting that were known reactions to Zyban, and when he ceased the drug, the headaches and vomiting stopped. It was at this time that he also developed Bell's Palsy. Due to the temporal relationship between the commencement of the drug and the onset of symptoms, Tim concluded that there was a relationship between the two:

> I'm certain within my mind that there's a connection simply because it was the only thing that had changed and the sicknesses that I'd had had only been when I was on Zyban and when I stopped Zyban I stopped getting headaches and I stopped throwing up and everything else that was happening.

It is useful to note at this stage, that Tim's medical practitioner believes the Bell's Palsy was related to a virus, and the headaches and vomiting experienced by Tim were partially related to the drug, but coincidently partially related to a virus; an opinion which is supported by the experts.

Edward had a four hour gap between commencing the drug, and the onset of symptoms. This relationship was confirmed in Edward's case, as he took a second dose after the initial symptoms had passed, and experienced a similar reaction. Medical practitioners refer to this as a rechallenge:

> I took one tablet…About four hours after I took it I was vomiting and then I went on from there dry reaching for about four hours.

Code	Drug	Who first suspected ADR?	ADRAC view of whether the symptoms are likely to be associated with an ADR.	Temp Relationship	Multiple instances	Past ADRs	Process of elimination
Tim C09	Zyban	consumer	Very Low	x			x
Edward C10	Efexor	consumer	High (suspect ADR in conjunction with another condition)	x	x		x
Irene C11	hydralazine	consumer, confirmed by medical practitioner	Very high			x	x
James C12	Panadeine Forte	consumer and wife	High	x	x		x
Joanna C13	Celebrex	consumer confirmed by GP	Very high	x		x	x
Bob C14	Vioxx	consumer, wife and daughter	Very Low/ Very High		x		x
Robyn C16	Sabril	consumer and husband confirmed by medical practitioner	Very high	x		x	x
Paul C17	Lipitor	consumer	Very high			x	x

Table 5-7 Consumer diagnostic decision-making

> I had rung the doctor in between and I said, "Will I call the [hospital]", he said "No it might be the drug". I tried Stemetil suppository and it had no effect whatsoever and he said, I rang him the next day and said, "I seem to have got over it" and he said "Right well leave it for 48 hours and try another one. Sometimes you get, only get the one reaction". That was the second disaster. The second one lasted a fortnight; bouts of vomiting and reaching went on for nearly a fortnight.

Edward's medical practitioner did not participate in the study, however the experts stated that they believe there is a high likelihood that the symptoms were associated with the drug, however they said that the symptoms were more severe than would be expected for an ADR, and suspect that there may have been another complication not identified by Edward.

Multiple instances of a drug associated with a set of symptoms

James' case differed slightly from Tim and Edward's cases. The first time he experienced the symptoms, there was more than one factor involved, multiple drugs including anaesthetic drugs. It was not until a situation occurred when the symptoms were, again, temporally related to the drug, in the absence of any other likely cause for the symptoms, that James and his wife suspected the drug. They used their observation of the temporal relationship, but also memory of similar symptoms in a past situation:

> I thought I've had these symptoms before and I thought back with my wife who's fairly methodical too and worked out that's what it was so because the symptoms were the same and it's only when I took it so right that's why I've been ill after those operations, it wasn't the general anaesthetic it was the Panadeine Forte so I must be allergic to Codeine.

Bob experienced the same symptoms several times. He initially came up with a hypothesis that the rash was associated with the garden, and then when he experienced the same set of symptoms, in a different context, he began to suspect a photosensitivity reaction to the sun, which lead him to suspecting the drug:

> And I thought, oh…I just had a scratch and I thought, it's something in the grass… a reaction….Like, after work in the garden, I was going down the garden of a night to water,

> then I started on the legs, you know, which I sort of blamed just being in the garden. But since then, it's definitely the sun.
>
> In the car, the sun coming through the window. That's happened several times. Well, even one day, I left work to pay a bill or I'm not sure now, but to go somewhere. It might have been the water board or something like that. By the time I got there I was scratching all around here (indicating leg). It was the sun just through the windscreen.

The temporal relationship was less clear, as Bob had ceased the drug but continued to experience the symptoms. As can be seen from Joanna's case a photosensitivity reaction can continue for several years after the drug has been ceased.

It is interesting to note that in this case, the link was made between the sun and the rash, however, no clear link was made between the drug and the photosensitivity. The experts differed in their opinion. One expert believed strongly that the symptoms were associated with the drug, and the second expert believed strongly that the symptoms were not associated with the drug.

Edward's case was clearer, because he took the medication, experienced a suspected reaction, took the medication a second time, and experienced the same reaction a second time, clearly indicating a relationship between the drug and symptoms.

Past experience with suspected ADRs

In Robyn's case, as a person with severe epilepsy, she had past experience with reactions to medications, and so when she experienced what appeared to be a severe epileptic fit, similar to psychosis, and due to the close temporal relationship between the commencement of the drug and the onset of the symptoms in the absence of any other drug or environmental changes, she suspected the drug. This suspicion, again, was confirmed by the experts.

Irene's case was significantly more complex, due to the large number of drugs she takes regularly. Irene, however, has experienced suspected reactions to medications many times, and maintains detailed diaries of medical consultations, drugs, drug dosages and symptoms. She appeared to use her awareness that drugs can be associated with symptoms, the Internet to

search for a link between the drug and the symptoms, and again the temporal relationship between the drug commencement and onset of symptoms, and very careful observation and recording of those observations in order to detect the link.

Irene's specialist confirmed that there is a high likelihood that the drug was associated with the symptoms. The interesting thing about this case was that Irene used observation, logic and reasoning to suspect the ADR, accessing medical information from the Internet to assist her, whereas the medical practitioner said that he did not suspect the ADR because the symptoms are not usually associated with the drug at doses so low. Irene was aware that she sometimes requires a lower than recommended dosage based on past experience and knowledge of herself, information not used by the medical practitioner.

Process of elimination

In each of these cases, an analytical process of eliminating other possible diagnoses occurred, leaving the suspected ADR as the final diagnosis in the minds of the consumers. For Tim, Edward, Joanna and Robyn, there had been no other significant change to their life style. In James case, the first time the reaction occurred there were other factors, such as surgery and anaesthetic drugs, but in the second case, these confounding factors were not present. In Paul and Irene's case, there was a process of considering alternative, and gradually eliminating them, until the suspicion of the drug was one of the few possibilities left. Both located information to support this growing hypothesis.

Skills used by consumers in the detection of suspected ADRs in the absence of medical knowledge

The skills used by these consumers to make these diagnostic decisions appear one or more of the following:

- a clear temporal relationship between the commencement of the drug and the onset of symptoms, the absence of any other possible cause such as another disease or other medications;
- a recognition from past experience;
- multiple experiences of the same drug/symptom relationship and;

- elimination of other possible diagnoses, leaving a suspected ADR as the final hypothesis.

Of the 15 cases, there were three where the experts and medical practitioners agreed that there was another diagnosis that was more likely to be associated with the newly presenting symptoms, than a drug. In these three cases, the knowledge used by the experts and medical practitioners was a broad knowledge of disease, information not available to the consumers. In the remainder of the cases, when the consumer was the first to suspect the ADR, the skills used by the consumer was sufficient to detect a suspected ADR. This illustrates the role of the consumer in the diagnostic decision-making, and the importance of making these diagnoses in conjunction with a medical practitioner.

5.5.1.2. Medical practitioner/consumer decision-making models

Medical practitioner/consumer decision-making models were discussed in the chapter two. To re-iterate, (Scott & Lenert, 2000) refer to four models of medical practitioner/consumer decision-making. Paternalistic, Informed, Collaborative or Deliberative models which originally were described by (Emanuel & Emanuel, 1992). Paternalistic decision-making is defined as a model where by the clinician has complete authority to make decisions on behalf of the consumer. Informed decision-making is defined as a model where the consumer makes completely autonomous decisions. Collaborative decision-making is defined as a model where the consumer relies on the health provider to provide information, but also to facilitate the decision-making processes. The final model is described as Deliberative. In this model, the health provider attempts to convince the consumer of the best outcome for their health, based on what the medical practitioner believes is in the consumer's best interests.

Each of the medical practitioners in the study have been classified into one of Emanuel and Emanuel's classifications in Table 5-8.

Description of the decision-making model	**Emanuel and Emanuel's model (1992)**
"Most people still say "what do you think?" "I'll go with your thoughts" And then you have to say "well if it was me, and you've done all these right things, and it's still there, I'd treat it." So more people are like that." "…sometimes you know you are in for a real fight about what you are going to do either to convince them to take it, or to convince them that they don't need to take it. And that's difficult too. And talking people out of it, when they think they need it."	Combination of collaborative and deliberative.
"[the model used included] a bit of both (medical practitioner and consumer) [the consumer] wanted to get to the bottom of why she had experienced the grand mal. She initiated going back onto the [the drug], and initiated checking her blood levels. She was concerned about losing her licence.	Combination of informed and collaborative
"[The medical practitioner's] normal style is to make a suggestion and for the patient to agree with it. He said he hopes he involves the patient in the decision-making process. He said it is important to get the patient involved as it impacts on compliance. In situations such as Cholesterol, the patient does not feel sick, they have to trust that if Cholesterol is not controlled now, there could be a major impact ten years down the track. It is particularly important to have patient compliance with these medications."	Collaborative, moving towards the deliberative model
"[One medical practitioner] feels that he is an advisor only. He described his role as to provide a service, and to provide guidance in decision-making, but that the consumer is the decision-maker ultimately."	Informed
"Yes, it's interesting actually, my [experience] is that often the patients have very firm views about it [the relationship between a drug and an ADR], and it's often the patients who make the decision rather than the medical practitioner."	Medical practitioner's view that consumers often use the Informative model. Unclear whether the medical practitioner agrees with this.
"And she just made a decision that she felt that the benefits of being on the [drug], weren't good enough for her to be able to keep on with it. So she was aware of that, and so she decided to stop taking the drug, which she did. She then went on to some other forms of homeopathy, to help her with her symptoms which she didn't fill me in on." "…she had already made up her mind because she stopped it the day before she saw me, so she had already made up her mind to get off the [drug], and therefore was not open to any negotiation really when she came in [laugh]. I think when someone stops a drug before they see a medical practitioner, it usually means they're serious about it. [laugh]. So no matter what I was going to say." "Well, look if it was her only treatment, for instance if she hadn't had chemotherapy, I would be wanting to change her onto something else"	Consumer using Informed model, Medical practitioner preferring the paternalistic or deliberative model.
"I think the patient presented with the symptoms and the medical practitioner quite reasonably concluded it might be the medications. I can't be sure that [the consumer] didn't come out and say "I've got joint pains and skin rash and I think it's my [drug]", but she might have. But [unintelligible] patients don't do that, patients tend to come out and say this is what's wrong with me, and it's usually a drug they've been taking for quite some time, and it's only in retrospect that it's realised it may be medication related."	Paternalistic

"…it gave us more options of things to try," [The medical practitioner's] use of "us" referring to himself and [the consumer], implies a partnership. "I certainly wouldn't have been giving her, because I know she likes to do things in as natural a way as possible, so I would not have been giving her an anti-inflammatory drug…in the first instance. You know I would have been suggesting she tried other means"	Collaborative as defined by us rather than Emanuel and Emanuel.

Table 5-8 Medical practitioner/consumer decision models based on Emanuel and Emanuel's (1992) model

Expansion of the medical practitioner/consumer decision-making model

Further analysis of the consumers and medical practitioner's decisions revealed seven classifications of medical practitioner/consumer decision models, expanding Emanuel and Emanuel's (1992) model. Some of the models suggested by Emanuel and Emanuel (1992) have been split into two models in the classifications listed below:

- Consumer decision-making with no consultation with medical practitioner.
- Consumer decision-making informing the medical practitioner of decisions.
- Consumer decision-making and the medical practitioner provides advice.
- Consumer and medical practitioners as partners in decision-making.
- Medical practitioner decision-making considering consumer preferences.
- Medical practitioner decision-making informing or convincing the consumer of the decisions.
- Medical practitioner decision-making with no consultation with consumer.

These have been described below using examples of decisions for illustration.

<u>Consumer decision-making with no consultation with medical practitioner</u>

This model includes decisions made by the consumer only. Once the consumer made the decision, it was not discussed with a medical practitioner for verification. This model, in combination with the following model is equivalent to Emanuel and Emanuel's (1992) Informed model.

James reasoned that he does not see his GP very often, and he is confident of his decision that the symptoms were related to the Panadeine Forte and Tramal. The experts agreed with his decision.

Kay made the decision, with the pharmacist to change brands of the drug sodium valproate, without consulting or informing her medical practitioner. It appears that she was not aware that monitoring this change may be important.

Consumer decision-making and informed medical practitioner of decisions

This model includes decisions where the consumer made a decision, and then informed the medical practitioner once the decision had been made. The decision was made with no consultation with a medical practitioner. This model, in combination with the previous model, is equivalent to Emanuel and Emanuel's (1992) Informed model.

Dr O'Neil said that Mary came to his consulting rooms having already made the decision to cease tamoxifen. She had ceased the drug the day before. She reported that she discussed it with him. From Dr O'Neil's perspective, Mary had made the decision independently, and informed him.

Another example of a consumer making a decision and informing the medical practitioner is when James informed the hospital that he had a reaction to codeine, but did not discuss with them the process of deciding whether he had or had not experienced an ADR.

Consumer decision-making and medical practitioner provide advice

In this model the medical practitioner acts as a consultant to the consumer providing information, but the consumer makes the final decision. This model is equivalent to Emanuel and Emanuel's (1992) Collaborative model.

In Paul's case, Dr Kent provided information about possible reasons for the set of symptoms Paul was experiencing. Paul was the person to make the decision to cease the Lipitor. Dr Kent

said that his usual model is a consultative model where he provides information to the consumer, but the consumer can make their own medical decisions.

Consumer and medical practitioners partners in decision-making

In this model, the consumer and medical practitioner work together in partnership, in a similar way to colleagues. This model does not have an equivalent model in Emanuel and Emanuel's (1992) system.

Dr Green said that he felt that in the hospital the decision-making model was of shared decision-making. He illustrated this point by referring to Kay's request for specific tests and asked to be put back on the Epilim brand of sodium valproate.

Julie was given a range of medications she could use to manage her pain. She had broad guidelines about which medication to use, when and the dosage. As long as she worked within these guidelines, she has a high level of discretion about the use of drugs. In this case, Julie was encouraged to make decisions about when to take certain medications, and the dosage she required at the time. Julie also said that when her GP was unsure about how to proceed, he would consult the specialist. It appears the team of medical practitioners were partners with Julie in managing her condition.

Joanna and Dr Carey worked together in an attempt to manage the suspected ADR. Throughout the interview, Dr Carey referred to "we", Joanna and himself when discussing the management strategies that were trialled.

Medical practitioner decision-making considering consumer preferences

In this model, the medical practitioner makes the decisions based on the consumer's preferences. This model is the equivalent of Emanuel and Emanuel's (1992) Paternalistic model. There are no examples of this type of decision-making in the data.

Medical practitioner decision-making informing or convincing the consumer of the decisions

In this model, the medical practitioner makes the decisions and either informs the consumer of the decision, or convinces him/her of the decision that has been made. This model is the equivalent of Emanuel and Emanuel's (1992) Deliberative model.

In Edward's case the medical practitioner provided reasoning as to why Edward could safely try the drug a second time, however the decision to take a second dose appeared to be the medical practitioner's decision, and he convinced Edward of his reasoning.

Another decision made in this style was the decision to commence the Efexor. According to Edward he did not feel he needed medication for depression however the medical practitioner made the decision and persuaded Edward to try the medication.

Kay's medical practitioner made the decision for Kay not to drive for a month following her epileptic seizure. This however was a medical decision guided by a law; a decision where the medical practitioner had no discretionary power beyond deciding if there was a likely cause for the epilepsy. In this case Kay was informed rather than consulted.

Medical practitioner decision-making with no consultation with consumer

In this model, the medical practitioner makes decisions with no consultation with the consumer. This is the equivalent of Emanuel and Emanuel's (1992) Paternalistic model.

In Kerry's case, she was in hospital for a surgical procedure. Decisions about the surgical procedure and which drugs would be used were made without discussion with Kaye, or informing her pre or post surgery. This is possibly a typical scenario in surgical cases. The complexity in Kerry's case was that due to her history of problems with anaesthetic drugs, she wanted to have a discussion with the anaesthetist prior to surgery, but due to the time constraints, was unable to do so.

The above examples suggest that the range of models suggested by Emanuel and Emanuel's (1992) can be expanded to include more models.

5.5.2. HOW DO DECISION-MAKERS CONTRIBUTE TO THE CREATION OF NEW KNOWLEDGE?

5.5.2.1. Individual decision-maker learning

New ADR knowledge can be generated at a national and international level. New knowledge and/or understanding can also occur at an individual decision-maker level. The analysis of the medical practitioner data suggested some problems surrounding individual learning.

Lack of feedback to prescribing and medical practitioners

In several cases, the clinician prescribing the drug was a different medical practitioner to the clinician treating the consumer.

In Irene's case, several GPs were involved in Irene's medical management while she was experiencing the reaction to hydralazine, but did not associate the symptoms with the drug. In this case the specialist prescribed the drug, but the consumer sought treatment from her GP rather than the prescribing medical practitioner. Once a diagnosis had been made by the specialist, it is not clear whether the GPs received feedback from this specialist.

In Joanna's case, she did not report her suspected reaction back to the prescribing clinician, and again, it is not clear if the medical practitioner sent a report to the prescriber or not.

James and Helen both experienced their suspected ADRs following surgery. Neither of them had a follow up visit with the surgeon or with a GP. Because they don't regularly need to visit a GP, they did not have an opportunity to report the suspected ADR back to the prescriber.

At the time of interview, Paul had not reported back to Dr Kent that he had ceased the Lipitor. He also had not reported that he had commenced an alternative non-drug treatment, and that he chose not to follow up on the referral to the orthopaedic surgeon.

In the preliminary background studies (O'Brien & Yearwood, 2002), an issue raised by the GPs in the GP forum, was that they do not perceive that they see ADRs frequently. In each of these cases, a prescribing or treating medical practitioner did not, or may not have received feedback

about the suspected ADR, affecting both their perception of the frequency of suspected ADRs, and their individual learning about the effects of drugs on particular individuals.

Lack of feedback to ADRAC impacts individuals learning

Another impact on individual learning is the lack of feedback to ADRAC.

Dr Carey believed he 'should' have reported the case to ADRAC. "…it is pretty slack not to report it". He went on, however to discuss his priorities, and the issues with the ADRAC reporting process as reasons for not reporting the suspected reaction. Given that this was a reaction that was unfamiliar to Dr Carey, it is likely that it will be unfamiliar to other GPs also. By not reporting the reaction, this information is not conveyed to the TGA to add to the national and international database, but also not highlighted for other individual GPs to assist in their learning.

5.5.3. SUMMARY OF COMBINED GROUP ANALYSIS

The combined group analysis section produced results that could be seen when viewing the individual case study and group analysis results together. This section revealed strategies consumers use when making diagnostic decisions surrounding ADRs, an expansion of Emanuel and Emanuel's (1992) medical practitioner/consumer decision-making model, and issues surrounding ADR reporting that impact on individual decision-maker learning.

5.6. Conclusion

This chapter has described results from the group analysis of the consumers, medical practitioners, and experts, and results from combining the group data with the individual case study data. The consumer analysis included analysis of the 15 consumer interviews plus the single interview of Joan's husband. The medical practitioner analysis included analysis of interviews from nine medical practitioners from eight of the case studies. The expert analysis included analysis of 30 questionnaires, two per case study. The combined group data analysis revealed results that emerged only when combining each set of data.

The results from these three levels of analysis, the individual case study analysis, the group analysis and the combined analysis, have been summarised below:

- These data suggest that consumers and medical practitioners make decisions surrounding ADRs, and the decision types made by each include diagnostic decisions, treatment decisions, information sharing and information seeking decisions. The medical practitioners also made decisions about prescribing and ADR reporting; two decision types not made by the consumers.

- The term 'side effect', 'reaction' and 'allergy' were terms used by the consumers, medical practitioners and experts. The medical practitioners also used the terms 'significant reaction' and 'significant side effect', terms not used by the consumers. The experts used the terminology defined by the World Health Organization (WHO). An additional term used by the experts is 'unexpected ADR'. Each group used these terms differently, and the difference appeared to result in miscommunication in some cases between the consumer and medical practitioner.

- The consumers and medical practitioners each used differential diagnostic strategies to determine if the newly presenting symptoms were associated with a disease or a drug. The medical practitioners appeared to either diagnose an ADR by using past experience and a pattern matching style of diagnosis, or hypothesising a number of possible diagnoses, and gathering information to strengthen or eliminate each hypothesis. The medical practitioners appeared to use their knowledge of medicine and disease to determine which disease/s was most likely to be associated with the set of presenting symptoms. The consumers used a different set of strategies to detect a suspected ADR, such as using the temporal relationship between drug onset and symptoms, multiple instances of a drug associated with a set of symptoms, past experience with ADRs and process of elimination.

- The consumers expressed that they would like more information about potential ADRs known to be associated with medications, and about the pre-existing disease. The

medical practitioners expressed a general concern that providing detailed ADR information to consumers may result in consumers either choosing not to take an essential medication due to their inability to weigh up the risks of taking a medication compared with the risks of not treating a disease. The experts said that for some cases, providing the consumers with warnings about suspected ADRs and/or written information about known risks of medications may have resulted in earlier detection of the ADRs.

- None of the suspected ADRs in this study were reported to ADRAC. The reasons provided by the medical practitioners included the reporting processes are complex and time consuming, the medical practitioner did not believe the symptoms experienced by the consumer were likely to be a suspected ADR, and that the ADR was well documented in the literature and well understood. In many cases prescribers and/or medical practitioners did not receive feedback from the consumer or medical practitioner once a diagnosis had been made, impacting on individual learning.

- Emanuel and Emanuel (1992) describe four medical practitioner/consumer decision models; paternalistic, collaborative, deliberative and informed. The data from this study have expanded on this model, and suggests the seven decision-making models, which will be discussed in detail in 6.3.2:

    - Consumer decision-making with no consultation with medical practitioner.
    - Consumer decision-making and informed medical practitioner of decisions.
    - Consumer decision-making and medical practitioner provide advice.
    - Consumer and medical practitioners as partners in decision-making.
    - Medical practitioner decision-making considering consumer preferences.
    - Medical practitioner decision-making informing or convincing the consumer of the decisions.
    - Medical practitioner decision-making with no consultation with consumer.

Each of these results will be discussed in the following chapter in relation to the pre-existing literature and the implications for consumers, medical practitioners and experts when attempting to prevent, detect and manage ADRs; and concepts to consider regarding decision support.

CHAPTER SIX

Discussion

6.1. Introduction

The previous two chapters described the results that emerged from three forms of analysis: analysis of the individual case studies; the groups of data; and the combined analysis. These chapters were structured according to the research questions. This chapter moves away from this structure so the results can be integrated into emerging theory that crosses multiple research questions.

Concepts are the building blocks of theory. The work of this thesis commenced with an understanding of some concepts within the ADR domain, which were described in chapter two.

This chapter begins with a discussion of the concepts in the ADR decision domain (section 6.2) which includes: concepts that were defined within this work to accommodate multiple perspectives; concepts with multiple definitions that were informed by the data; and concepts with single definitions that have been applied to a domain with multiple perspectives. This is then followed by a discussion of the contributions this work has made to theory (section 6.3). These contributions include: the use of multiple perspectives and triangulation to inform systems design; medical practitioner/consumer decision models; ADR differential diagnosis; the role of the consumer in ADR decision-making; problems with generating new ADR knowledge; and ADR decision-making based on partial knowledge as a contributor to the incidence of ADRs. The final section of this chapter, section 6.4 is a discussion of the limitations of this work.

6.2. Concepts in the ADR decision domain

The concepts from the ADR domain, which were described in chapter two, were defined from a medical perspective. An example is the concept of an ADR which was defined according to the World Health Organization (WHO) definition.

The positivist theoretical perspective that has underpinned past work within this domain has the focus of finding a single understanding of core concepts. The use of a symbolic interactionist theoretical framework, not only permits, but expects any concept or symbol within a specific domain to have different meanings for different groups.

The methodology used within this work, and in particular the collection of three perspectives of a single instance of an ADR has provided additional insight into many of these concepts due to this addition of multiple views of each concept. A contribution of this work, therefore, is an expansion in understanding of some of the core concepts in this domain, and in particular the move from a single understanding to multiple understandings of some concepts.

Each of the primary concepts used within the ADR decision domain has been listed in one of the four tables below, including a brief definition. The concepts have been divided into four groups, which are represented by four tables. The first table (Table 6-1) includes the actors or decision-makers within the ADR domain. This group of concepts were discussed in chapter two and so will not be discussed further in this section. The second table (Table 6-2) includes concepts that have been defined by the study to accommodate multiple perspectives. The third table (Table 6-3) includes concepts that have been defined by the preliminary background work and the literature. These concepts began with a single meaning but have been informed by this work, providing a new understanding based on the multiple views obtained within the data. The fourth and final group (Table 6-4) also includes concepts that have been defined by the preliminary background work and the literature that began with a single meaning, but when used across multiple groups with this assumed single meaning appear to add to miscommunication between decision-makers. A discussion of the contribution this work has made to the understanding of these groups of ADR decision domain concepts follows these tables.

Actors or decision-makers in the ADR domain	Brief definition
Consumer	The purchaser and/or recipient of medical services
Medical practitioner	A 'doctor' who has been consulted by a consumer for a medical condition. Includes a GP, specialist, or medical practitioner working in a hospital setting.
Expert	A member of the Australian adverse drug reaction advisory committee (ADRAC) who has agreed to participate in this study as an ADR expert.
Pharmacist	Within the context of this work, a pharmacist refers to a community pharmacist who has been consulted by a consumer.

Table 6-1 Actors or decision-makers in the ADR domain

Concepts that accommodate multiple perspectives	Brief definition
Suspected ADR	A set of symptoms that any decision-maker believes may be associated with a therapeutic drug

Table 6-2 Concepts that were defined to accommodate multiple perspectives

Concepts that have been informed by the data that have multiple definitions	Brief definition
Adverse drug reaction (ADR)	Refer to section 6.2.2.1 for a detailed discussion of this concept
Side effect	Refer to section 6.2.2.1 for a detailed discussion of this concept
Allergy	Refer to section 6.2.2.1 for a detailed discussion of this concept
ADR decisions or decision types	Refer to section 6.2.2.3 for a detailed discussion of this concept
ADR decision-maker	Refer to section 6.2.2.2 for a detailed discussion of this concept
Diagnosis	The most likely explanation for a set of symptoms. This concept will be defined further when discussed in the section 6.3.3 on emerging theory of ADR diagnosis.
Differential diagnosis	Determining which of two or more possible explanations for a set of symptoms is most likely. This concept will be defined further when discussed in the section 6.3.3 on emerging theory of ADR diagnosis.
Impact of an ADR	Refer to section 6.2.2.4 for a detailed discussion of this concept
ADR context	Refer to section 6.2.2.5 for a detailed discussion of this concept

Table 6-3 Concepts with multiple definitions that were informed by the data

Concepts with single definitions that add to ambiguity in a domain with multiple decision-makers	Brief definition
Known ADR	Symptoms associated with a therapeutic drug that have been documented
Unknown ADR	Symptoms associated with a therapeutic drug, that have not yet been documented.
Preventable ADR	An ADR caused by a drug being prescribed to a consumer with: A known contra-indication A known allergy to the drug or class of drugs A drug known to cause an interaction with another drug the consumer is concurrently taking.
Allergy – known	A consumer has experienced an allergy to a particular drug or class of drugs in the past.
Allergy – unknown	An allergy a consumer has to a drug, which has not been identified or documented.
Contraindication	A drug that either 'should not' or 'must not' be taken by a consumer with a particular condition.
Drug interaction	Drug interactions are ADRs that may be caused by a drug/drug interaction, or a drug/food interaction (Kalachnik, 1999).
Medical error	Misdiagnosis Improper choice of treatment Failure to avoid drug interactions Failure to detect if the drug treatment is not working Failure to detect if the drug is causing further injury Failure to avoid allergic reaction (Woodstock, 2000)
Compliance	Term used by the medical practitioner, which refers to whether a consumer follows a regime either constructed by the medical practitioner, or constructed through a collaborative process between the medical practitioner and consumer.
Nocebo effect	"…'non-specific side effects' are symptoms or physiological changes that cannot be explained on the basis of the known pharmacology of the drug and are idiosyncratic and not dose dependent. In theory non-specific side effects may be positive and beneficial or negative and adverse" (Barsky, Saintfort, Rogers & Borus, 2002).

Table 6-4 Concepts with single definitions applied to a domain with multiple perspectives

6.2.1. CONCEPTS THAT WERE DEFINED TO ACCOMMODATE MULTIPLE PERSPECTIVES

In this work, there was a single concept that was defined to accommodate multiple perspectives; a 'suspected ADR'. Rather than defining an ADR based on the initial WHO definition, a decision was made to allow the consumer who volunteered for the study to determine if s/he has experienced a suspected ADR. By beginning with a single perspective from one of the

participant groups, one definition and explanation of that definition was collected initially. By then asking the medical practitioner/s and then experts whether they agree with the consumer perspective, a second and third perspective of the definition of an ADR emerged. Not only did the definition emerge, but the beliefs and reasoning behind the definition emerged.

6.2.2. CONCEPTS WITH MULTIPLE DEFINITIONS THAT WERE INFORMED BY THE DATA

6.2.2.1. ADR, side effects and allergies

The data that informed the concepts 'ADR', 'side effect' and 'allergy' and the results were presented in section 5.2.3.

To summarise, the experts, representatives of ADRAC, use the World Health Organization definition of ADR, and view the term 'side effect' as an outdated term that is better replaced with the term ADR. They refer to 'serious' and 'unexpected' ADRs to describe the subset of ADRs they are most interested in collecting via the spontaneous reporting processes.

The medical practitioners in the case studies used the terms 'reaction' and 'side effect'. They also referred to 'significant reactions' and 'significant side effects'. Although some of the medical practitioners made comments indicating there was a difference in meaning between these terms such as "I'm not sure if there was a reaction, but I just think she was certainly having side effects …" the use of each term within the case studies did not reflect this. The use of the word 'significant' appeared to be what determined if the medical practitioner needed to act upon the set of symptoms by either treating them or withdrawing the drug, regardless of whether s/he was referring to a 'reaction' or 'side effect'.

The consumers appeared to refer to a 'reaction' as something a person experienced and a 'side effect' as an attribute of the drug but otherwise used the terms interchangeably.

It appears from the data that despite the differences described, each group use the terms 'side effect' and 'reaction' to mean non-therapeutic symptoms associated with a medication. In the cases when a participant attempted to differentiate between the terms, it also appeared that the term 'side effects' referred to the symptoms expected or known to occur in some people with a

particular reaction, and 'reaction' as something unexpected or more serious, however this was not consistently apparent. To take this further, a 'significant side effect' may mean a known and expected ADR that a consumer cannot or chooses not to tolerate, and a 'significant reaction' may mean an unexpected or less predictable reaction that resulted in a change of treatment.

The consumer appeared to have a general term for "non therapeutic symptoms associated with a drug", that is, some thing is happening that should not be happening. The medical practitioners appear to be more specific, with a clear distinction between 'allergy' and a more general term of 'side effect' or 'reaction', and with the qualification of 'significant'. The experts, however, had a specific definition, classifying ADRs as Type A to E and including contraindications, interactions and product manufacturing faults, also as important information.

The formal product information found in electronic prescribing products refers only to adverse drug reactions, (Medical Director, 2003). The *Consumer Medicine Information* (CMI) (*Better Health Channel*, 2003) refers to 'side effects', implying a side effect is a more general term and 'adverse drug reaction' a more medically based term.

When attempting to determine the incidence of ADRs, terminology differences between adverse drug reactions, adverse drug events, adverse events, medication errors and medical errors, were used inconsistently in the literature.

The term 'allergy' appeared to be used by all participants as a sub type of either 'reaction' or 'side effect' related to a hypersensitivity reaction to a particular drug.

It appears, therefore, that the definition of these terms is broad rather than precise, and that the general meaning of these terms is similar between participants. The problem in communication appeared to be when one participant was more specific in his or her usage of the term, such as when Mary approached her medical practitioner with what she believed was a suspected reaction, and he said "no, not a reaction, but could be a side effect". Another example is when one of the medical practitioners referring to the problem of providing consumers with ADR information said:

> I see far more of the anxiety from the person that comes in with the sheet, having underlined every symptom and, if they've taken it, I've had that, that, that and that, and most of those are not allergies, they're nausea, and some tummy upset, that's quite possible without an allergy, but it's difficult to know, sometimes if they are truly allergic, or whether they're getting some significant side-effects.

The consumer in this example, appeared to be saying s/he was experiencing some new symptoms, "nausea and tummy upset", but labelled them as an 'allergy'. The medical practitioner appeared confused because the consumer's description, in his mind, was not an 'allergy'. If the medical practitioner heard this as 'something is wrong and I think it's related to my medication' rather than specifically an allergy, the communication may be clearer.

The data found in these case studies cannot provide a definitive understanding of these terms. It can, however, provide some insight into how the terms appear to be being used, and suggest some problems that may be occurring due to differences in terminology between groups, when there is an expectation of a single understanding.

In the few case studies where a consumer or medical practitioner was asked about the definition, their response did not match their usage, indicating they are not cognitively aware of their usage of these terms. It is unlikely, therefore, that a study designed to specifically ask participants how they use the term, would provide data on their actual use of these terms, only what they believe they understand. In order to learn more about the inconsistencies in these terms, a study would need to be designed specifically to elicit the use of these terms.

The development of decision support within this domain using a positivist framework may result in a solution that involves choosing a single definition or understanding of these terms, and educating all ADR decision-makers to have a single understanding. This idea has been illustrated in Figure 6-1.

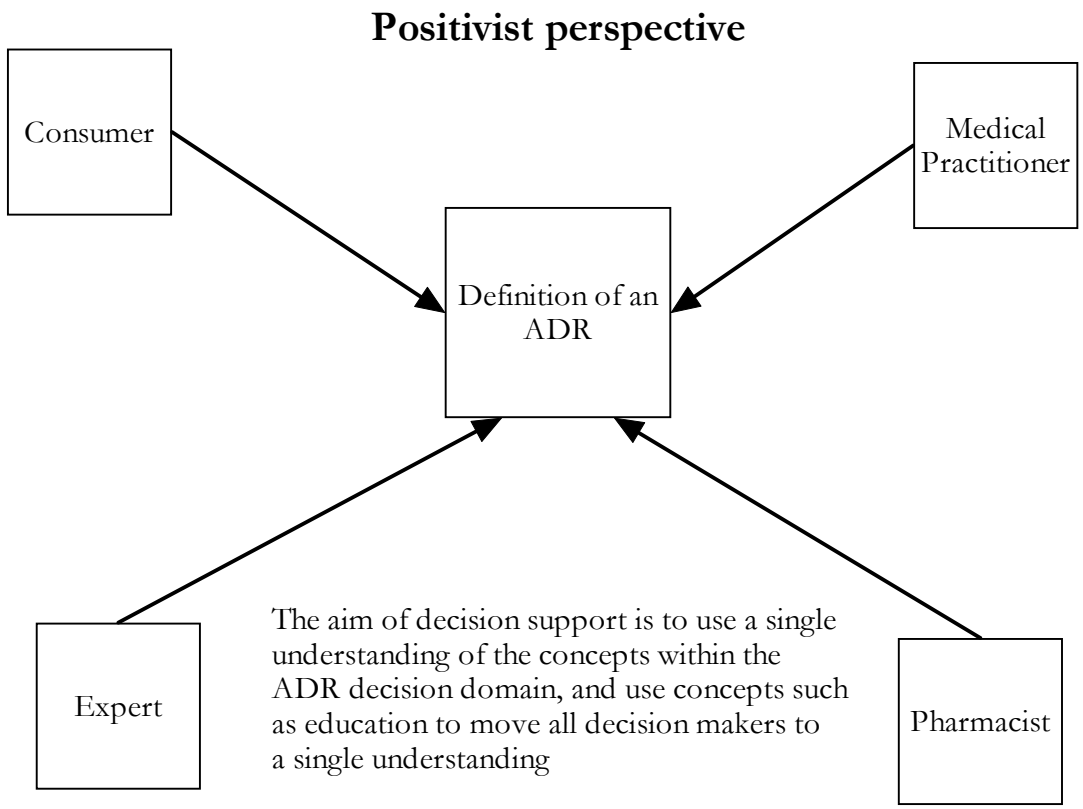

Figure 6-1 Positivist theoretical framework to develop decision support

The development of decision support using a social constructionist epistemology, and symbolic interactionist theoretical framework, however, points to a solution of accepting and valuing the diverse range of understandings, and encouraging ADR decision-makers to recognise different people use the same terms for different meanings.

One of the fundamental aspects of symbolic interactionism is that meaning is created through interaction with other members of the social group. The interaction, in many of the case studies, between the medical practitioners and the consumers was limited, limiting the opportunity to develop a shared understanding. Rather than making an assumption about the meanings, taking the time to understand what the individual consumer or medical practitioner means by each term, may be a role for ADR decision support. This notion has been illustrated in Figure 6-2.

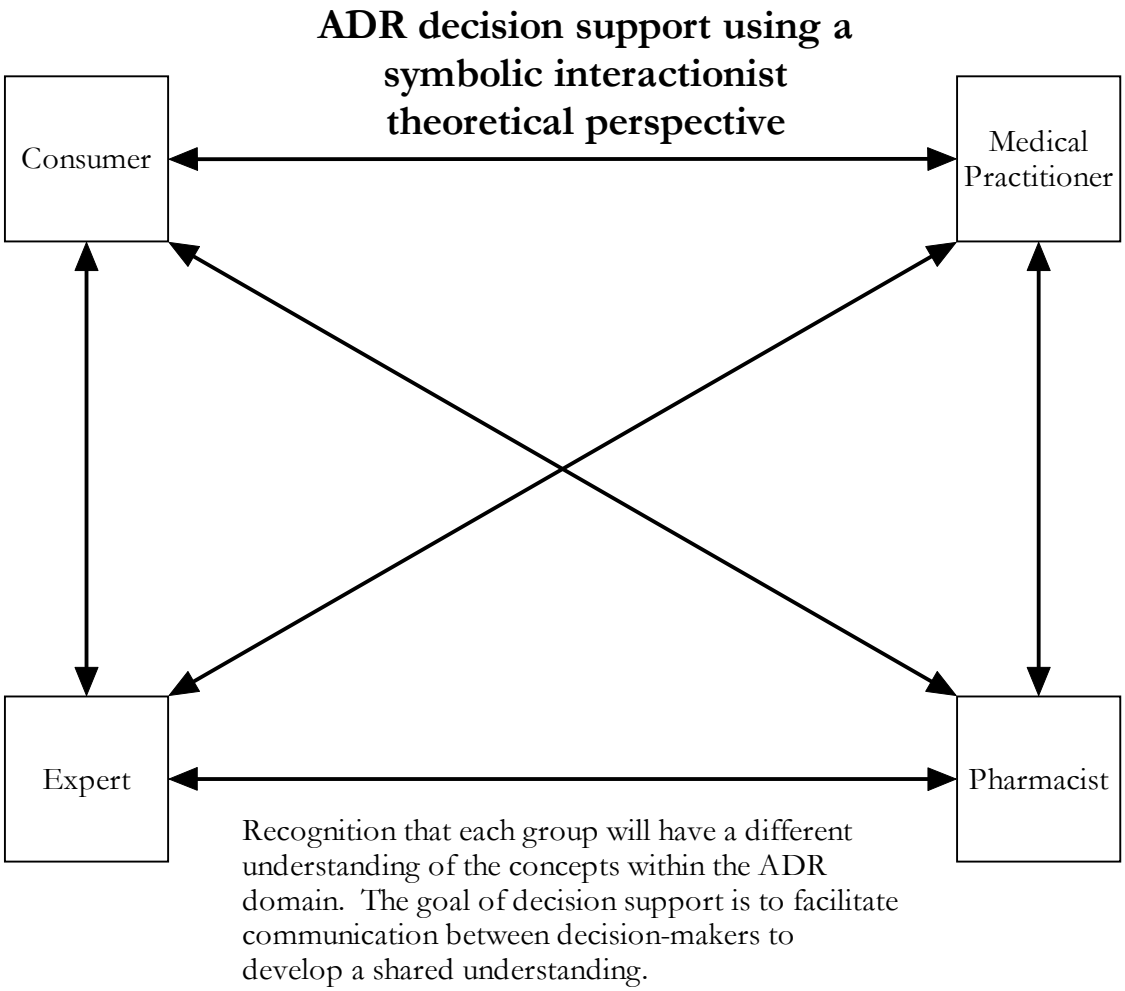

Figure 6-2 Symbolic interactionist theoretical framework to develop decision support

6.2.2.2. Decision-maker/s

The literature review identified a number of methods that have been used to reduce ADRs. We classified these into five groups in chapter two. They are: drug surveillance programs in Australia; drug surveillance at an international level; computerised clinical guidelines; incorporating decision support modules into prescribing software tools; early warning ADR systems that are hospital based; and increasing awareness, through education and training. These systems focused primarily on supporting decisions from a single perspective, the perspective of the medical practitioners. The results of this study as discussed in section 5.2.1, indicate that the medical practitioner is only one decision-maker in a decision domain that includes many different decision-makers including the consumer, the consumer's family and friends, and to a

lesser extent, community pharmacists and other health professionals such as naturopaths. This has been illustrated in Figure 6-3. The dotted lines indicate infrequent communication.

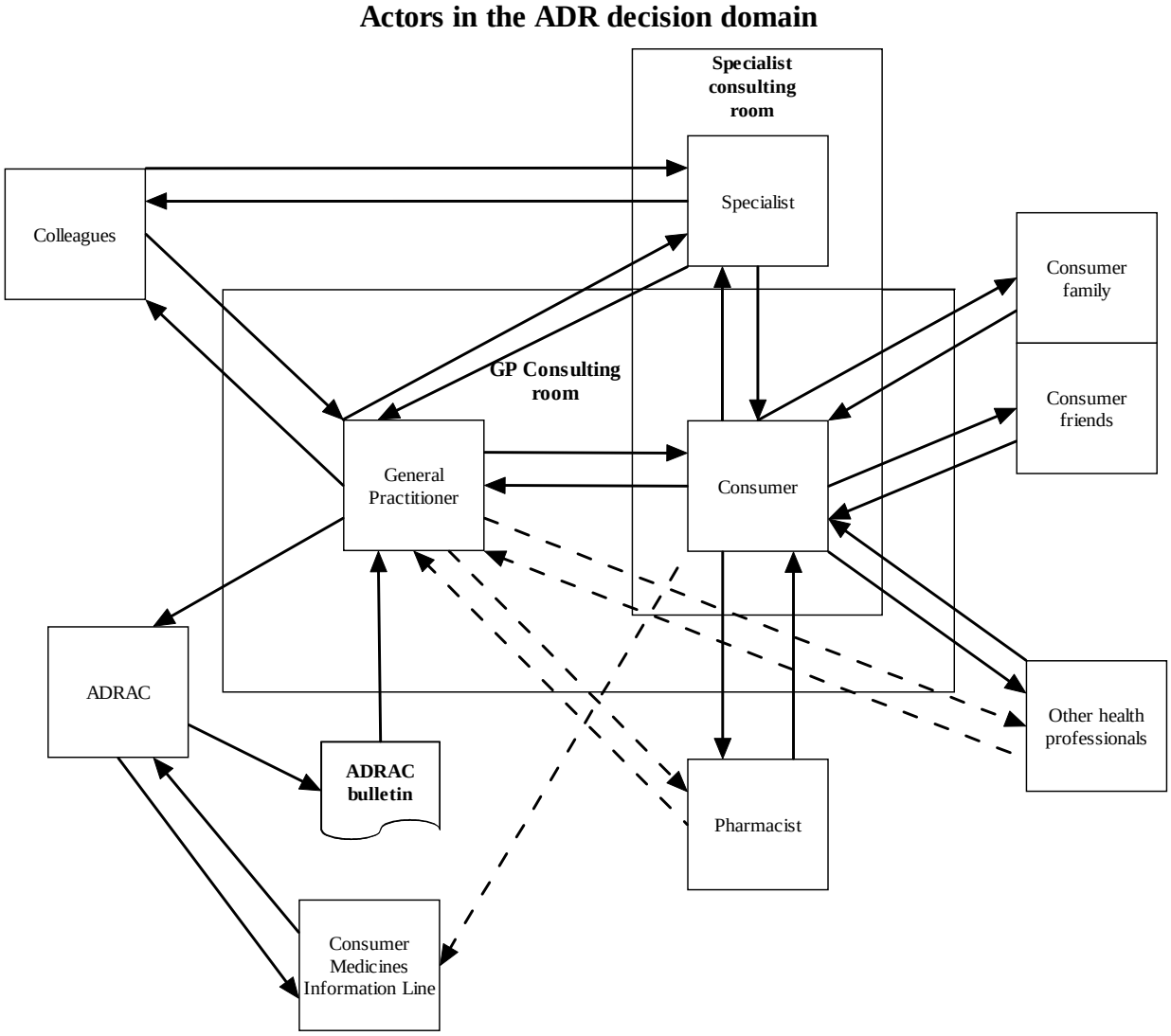

Figure 6-3 The actors or decision-makers in the ADR decision domain

The focus of providing ADR information and resources to prescribers, and building decision support to assist with the medical practitioner's decisions, appears to be a group of ADR solutions that are tailored to only part of the decision-making team, and only supporting some of the ADR decisions, which is likely to result in a partial rather than a complete decision support solution.

6.2.2.3. ADR decision types

The group analysis of the consumer data indicated that not only are consumers involved in the ADR decision domain, they play a significant role in this area, making a wide variety of decision types surrounding ADRs.

Decision types made by the consumers in this work (described in section 5.2.2) included diagnostic decisions, treatment decisions, decisions about which information to share and what information to seek. The medical practitioners also made a variety of decisions (described in section 5.3.1) including the four types of decisions made by the consumers and decisions about ADR reporting and prescribing decisions. Although the consumers cannot prescribe drugs, and so did not make prescribing decisions, they do make decisions about treatment, and so have input into prescribing decisions. The consumers in these case studies did not report their suspected ADRs, however, the introduction of the consumer medicines information line (section 2.2.6.9) has resulted in Australian consumers taking a larger role in ADR reporting. The pharmacists were primarily involved in the role of providing information to the consumer. The consumer's family and friends assisted the consumer with each of their decision types. Although there are variations in the actual decisions and the sources of information used by the consumers and medical practitioners, the role division is not as significant as the literature suggests.

There is a growing body of literature about the consumer role in medical decision-making, which was discussed in chapter two. Within this body of literature, there is beginning to be a focus on consumer decision support. This literature however focuses almost exclusively on treatment decisions. This study suggests that treatment decisions are only one decision type made by consumers, and that consumers play an important role in the detection and diagnosis of ADR decisions, challenging the belief that decision support for consumers will be restricted to treatment decisions.

6.2.2.4. Impact of an ADR

The concepts described in the previous section relate to understandings at a group level. That is, what the consumers understand compared with what the medical practitioner's understand. These next two sections, the impact of an ADR, and the importance of life context are related to

the individual circumstances surrounding an individual consumer, rather than consumers as a whole.

The GP forums conducted in the preliminary background work (O'Brien, 2001) revealed an informal scale used by medical practitioners to indicate severity of ADRs. This was a factor the GPs considered important to include in ADR decision support, so the prescriber was aware of the likelihood a severity of each ADR associated with a medication. This information could then be used to asses the risks associated with the drug compared with the benefits of the drug for a particular consumer. This terminology arose from forums with a single group of decision-makers, the GPs.

The consumer group data revealed another dimension related to severity, and that was impact of the ADR on the consumer. These results were discussed in section 5.2.6. To summarise these results, the impacts included:

- the immediate impact of a suspected ADR. For example, in Kerry's case she experienced a suspected reaction to Maxolon; double vision following surgery which resolved to blurred vision that lasted several days;
- the impact of a drug after the drug has been ceased. For example, in Joanna's case, she continued to experience a photosensitivity reaction for several years after having ceased the suspected drug;
- the impact on trust in drugs and/or medical procedures. For example, in Belinda's and Kerry's cases, there was significant fear of future surgery, due to past incidences of ADRs whilst undertaking surgical procedures;
- the impact on lifestyle. For example, in Joanna's case, again, her holiday was cut short, and her enjoyment of outdoor activities was affected by the continuing effects of the ADR.

The second aspect of severity and impact that was highlighted by the data was the differences in perceptions between decision-makers about the impact the suspected ADR had on the consumer. Two cases that illustrate this point are:

- Toni's case where the medical practitioner believed Toni recovered quickly from the suspected ADR to Tegretol, based on the fact that Toni did not go back for further consultations. Toni said that she did not feel completely well for ten weeks.
- Paul's case, where the medical practitioner believed the impact of the suspected ADR on Paul was at the level of an irritation, where as Paul was extremely distressed and felt his quality of life had been significantly affected.

In this second case, Dr Kent said that if he believed the ADR had been a problem to Paul, his management would have been different. To Dr Kent, the symptoms were low grade, and general indicating a low level of severity. To Paul, the symptoms were insidious and constant, affecting his sleep and impacting his overall quality of life.

The dimension of 'impact' emerged from the consumer data. The term 'severity', used by the medical practitioners, was a less complete indicator of the level of intervention required than the terms 'severity', from the medical practitioner data and 'impact', from the consumer data, when used together.

6.2.2.5. ADR context

Some of the factors that are likely to impact on a consumer are known prior to commencing a drug, some impacts cannot be known until the consumer is actually experiencing a suspected ADR. The previous section discussed the importance of understanding the impact of an ADR on the consumer. This section explores the factors known about the consumer prior to prescribing a drug that may be important to take into account when weighing up the risks and benefits of drugs versus treatments. The results that relate to context have been written in section 5.2.6.2.

To summarise, the key factors included the following:

- Whether the drug in question is essential or non-essential. If a drug is considered essential, there may be an increased chance that a consumer is prepared to accept the risk of an ADR, than for a non-essential medication. In Julie's case, drugs and combinations of drugs that

assist in managing her pain are essential for her to participate in her daily activities. She is tolerant, therefore of some irritating but minor ADRs such as tinnitus.

- Whether the person has had negative experiences with drugs in the past. A consumer who has a significant fear of experiencing further ADRs may be less prepared to risk an ADR in the future. In Kerry's case, she has had so many negative experiences with surgical procedures which were drug related, that her preference would be to have no surgery than to risk another potential ADR.

- Whether the person has factors in his or her life that would be severely impacted if an ADR were to occur. In Edward's case, the ADR not only had an impact on his own health, it had an impact on his ability to care for his wife with a severe disability.

These three factors have been illustrated in Figure 6-4.

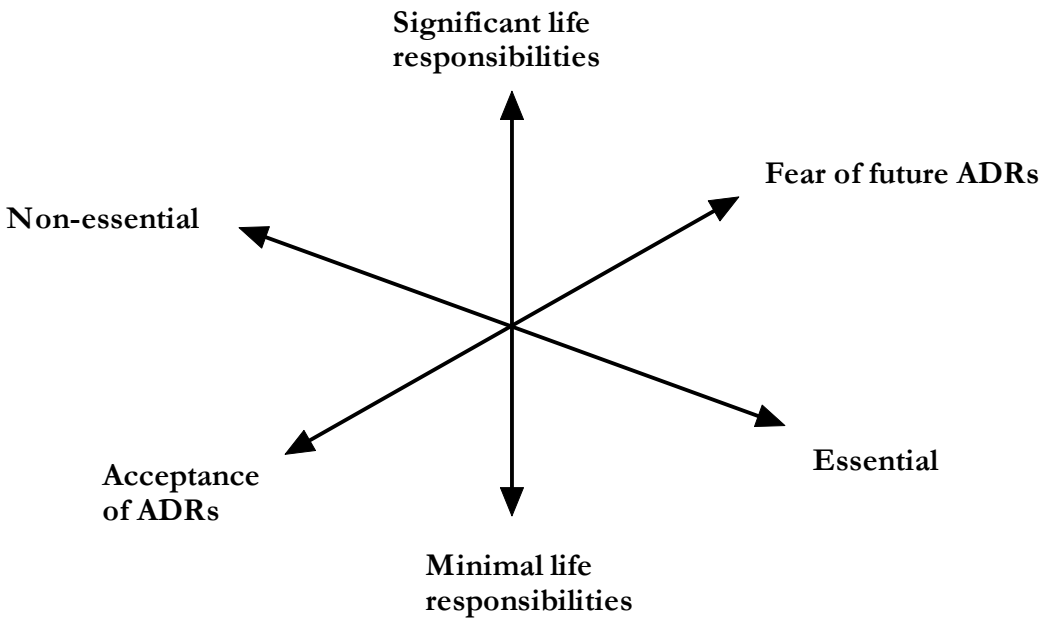

Figure 6-4 Life context factors to consider when weighing up the risks versus the benefits of a drug therapy

The development of weighted factors surrounding risk may bring to consciousness some of the factors that need to be considered when weighing up the risks versus the benefits of drugs, which may be useful when designing a decision support system, or may just be useful to facilitate a discussion between the consumer and medical practitioner about risk and benefits.

6.2.3. CONCEPTS WITH SINGLE DEFINITIONS THAT ARE APPLIED TO A DOMAIN WITH MULTIPLE PERSPECTIVES

Some concepts within the ADR decision domain have either not been defined clearly, or defined with the assumption that there is a single definition. This assumption has created ambiguity within this multi-decision domain. These concepts and the resulting lack of clarity have been described below.

6.2.3.1. Known and unknown

The concepts, 'known' and 'unknown' have not been clearly defined in the literature, but are used as the basis of many other concepts. Each of the definitions of ADR types that were described in section 2.2.1, use the term 'known' as a component of the decision. An example is the definition of a Type A reaction. "Predictable events or reactions, pharmacological reactions or expected events or reactions. Type A reactions are common and are accounted for by a drug's **known** pharmacological properties" (Kalachnik, 1999). The concepts of 'known allergy', 'unknown allergy', 'medical error', 'preventable ADR', 'contraindication', and 'drug interaction' are also all based on an understanding of what is 'known' or 'unknown'.

The implicit definition of what is 'known' is that knowledge has been discovered about an aspect of a drug and/or ADR associated with a drug, and that this knowledge has been documented. It is not clear where this new knowledge needs to have been documented in order for it to be considered 'known'. The second aspect of this definition which is ambiguous is when 'known' is applied to another definition, such as a 'known drug interaction'. Drug interactions were described in section 2.2.4.4. In summary drug interactions may be classed as pharmacokinetic or pharmacodynamic, resulting in an increased or decreased blood level or tissue level of the drug/s, or an additive effect. The complexity is when classifications of 'medical error' or 'preventable' come into play. If a medical practitioner prescribes a drug for a consumer which interacts with another drug the consumer is currently taking, resulting in a 'known' reaction, this

is considered according to Woodstock's (2000) definition, as medical error, and is also considered preventable.

The significant question in this situation, however, is 'known by whom?' Where does this information need to be located for a consumer and/or medical practitioner to have access to this information? If it is 'known' but in a location not accessible to the decision-makers, can it still be considered a preventable ADR? It could be considered a preventable ADR if the information about this interaction was available to the decision-makers at the time of making a decision.

An issue raised in the GP forums conducted as a part of the preliminary background studies (O'Brien & Yearwood, 2002, 2005), and has been re-enforced in recent health informatics conferences, is the difficulty the medical community are having, maintaining up to date knowledge, due to the increasing number of publications within this area. This problem adds to the ambiguity of what is considered 'known'.

This lack of a clear definition or set of definitions of the terms 'known' and 'unknown' has resulted in ambiguity surrounding the terms that build on these concepts. Further work is required to clarify these core concepts.

6.2.3.2. Compliance

Compliance was a term used by the medical practitioners, but was not used by the consumers. It appears to be a concept that fits within some of the medical practitioner/consumer decision models (described in section 6.3.2), but a term that does not fit within other models.

The term compliance was defined in the results section (section 5.3.4.2). To remind the reader, the term compliance was used when a medical practitioner made a recommendation for treatment, and the consumer did not follow, or 'comply' with that recommendation. A consumer is said not to comply, when they choose not to follow either the recommended, or the agreed course of action.

The consumer did not have an equivalent term. The consumer spoke of making various choices, and/or making decisions. The term compliance only holds where there is an assumption that

the medical practitioner is the primary decision-maker, and it is up to the consumer to follow what is recommended. When the assumption is made that the medical practitioner is an advisor who works with the consumer to make decisions, and that both parties have the right to make decisions, 'non-compliance', becomes, 'the consumer changed his or her mind' for some reason; a reason that may or may not fit with medical 'best practice', but makes sense to the consumer in some regard which may or may not be medically related.

The use of this term is inconsistent with our definition of a partnership in decision-making.

6.2.3.3. The nocebo effect

The nocebo effect or nocebo phenomenon is a term used within the literature, but was not used by any of the participants within this work. The concept underlying these terms, was used by the medical practitioners and alluded to by the consumers, however they did not attach this label to it. This term is discussed in detail when describing ADR differential diagnosis, and so will not be described here.

6.3. Contribution to theory in the ADR decision domain

In the previous section, the concepts, or building blocks within the ADR decision domain have been discussed. The use of these building blocks to form and develop pre-existing theory will be described in this section.

The level of theory derived from this work matches Merton's middle range theory (Blaikie, 2000). According to Blaikie (2000), Merton developed the middle range theory as a solution to a trend of social research where the focus of theory development was to either develop grand theories, which aimed to generalise to an entire society; or micro theories, that did not generalise beyond the immediate work.

The theory discussed in this section was derived from work which has focussed on the very specific domain of ADR decision-making. The emerging theories, however, tap into current more substantive theories within the domains of decision theory and decision support.

This work contributes to theory development in the following areas:

- the use of multiple perspectives and triangulation to inform systems design;
- medical practitioner/consumer decision models;
- ADR differential diagnosis;
- the role of the consumer in the ADR decision domain;
- ADR decision-making based on partial knowledge as a contribution to the incidence of ADRs;
- creation of new ADR knowledge.

Each of these will be discussed in detail in the following sections.

6.3.1. THE USE OF MULTIPLE PERSPECTIVES AND TRIANGULATION TO INFORM SYSTEMS DESIGN

The methodology used within this work to inform the pre-requirements analysis phase of systems design was a grounded theory analysis of case studies. Each of these case studies included multiple views of a single ADR. The underlying epistemology was social constructionism with a symbolic interactionist theoretical perspective.

The development of ADR decision support systems have used knowledge of the ADR decision domain that was primarily based on the perspective of the prescriber. The methodology used within this work to inform the requirements analysis phase of decision support development, provided insight based on the perspectives of the consumer, medical practitioner and expert. Knowledge that was developed using a single perspective and based on a single understanding has been developed to include multiple perspectives and to create multiple understandings which has resulted in a significantly greater insight into this decision domain.

Knowledge of the ADR domain was primarily situated in a positivist school of thought. The use of a social constructionist school of thought in combination with triangulated data, has lead to increased understanding of the differences between decision-makers, and the contribution of

those differences to the misunderstanding that occur within this domain and their contribution to the continuing incidence of ADR.

The work of this thesis has made progress towards the development of theory underpinning ADR decision-making, providing a solid basis for the development of ADR decision support. Further work will be required to consolidate and test this theory. The grounded theory approach provided a method of eliciting new theory within this domain.

A requirements analysis exercise elicits information that can be used to develop information systems, based on assumptions about the industry, such as who the key stakeholders are, and their primary information needs. Development of decision support may rely on the existence of theory and a detailed understanding of the decision domain. Traditional requirements analysis methodologies do not explore the decision domain in this level of detail.

The research methodology used within this work, therefore, has contributed significantly to the understanding of the ADR decision domain providing a solid basis for the development of ADR decision support that is grounded in theory that has been derived from real world data.

The following sections discuss the emerging theory that either expands on current theory, or contributes a new understanding, that has arisen from this research approach.

6.3.2. MEDICAL PRACTITIONER/CONSUMER DECISION MODELS

A medical practitioner/consumer decision model developed by Emanuel and Emanuel (1992), was first discussed in chapter two. Figure 6-5 is a graphical representation of this model, including the percentage of consumers who prefer each of these models based on Scott and Lenert's (2000) work. It is important to note that these models are based on how medical practitioners and consumers currently make medical decisions, not based on what is considered 'best practice'. These models, therefore, are based on Carroll and Johnson's (1990) definition of descriptive decision theory.

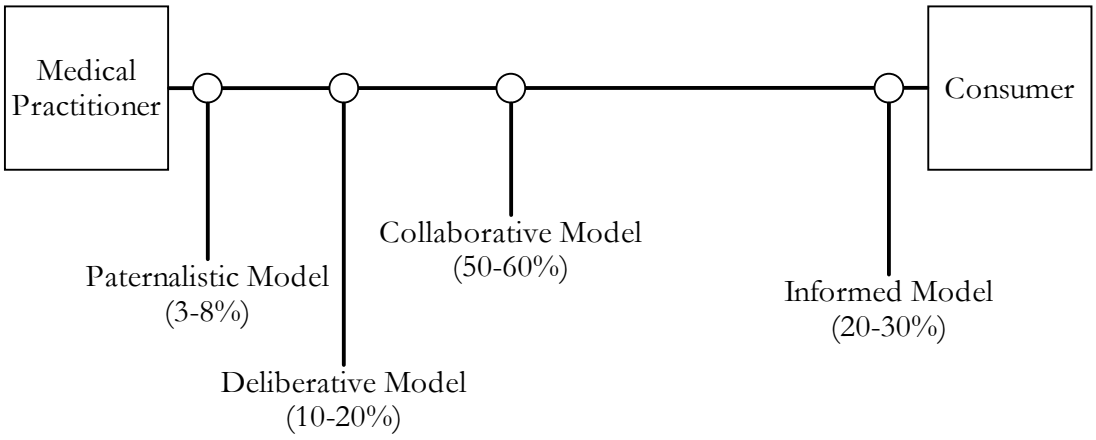

Figure 6-5 Medical practitioner/consumer decision-making models described by Emanuel and Emanuel (1992). The percentage of consumers who would prefer each model from Scott et al.'s (2000) work.

To remind the reader, Emanuel and Emanuel (1992) defined each of these models as follows:

- **Paternalistic decision-making** is defined as a model whereby the clinician has complete authority to make decisions on behalf of the consumer.
- **Informed decision-making** is defined as a model where by the consumer makes completely autonomous decisions. The role of the clinician is to provide medical information, but it is assumed that the consumer is responsible for determining their own preferences, and making the final decision.
- **Collaborative decision-making** is defined as a model where the consumer relies on the health provider to provide information, but also to facilitate the decision-making processes.
- **Deliberative decision-making** is defined as a model where the health provider attempts to convince the consumer of the best outcome for their health, based on what the medical practitioner believes is in the consumer's best interests.

Charavell et al.'s (2001) expansion of these decision models was also discussed in chapter two. They viewed the paternalistic and informative models described by Emanuel and Emanuel (1992) as reducing the exchange of information, where as the collaborative and deliberative

models attempt to increase the exchange. They suggested an additional model, the shared decision-making model, which sits between the collaborative and deliberative models. This new model includes the medical practitioner conveying information about the condition, including risks and benefits of various options to the consumer. The medical practitioner would elicit preferences from consumer and assist in the decision-making process, and also state their own preferences for the consumer. Charavell et al.'s (2001) suggestion has been incorporated into the figure illustrating the medical practitioner/consumer decision models in Figure 6-6.

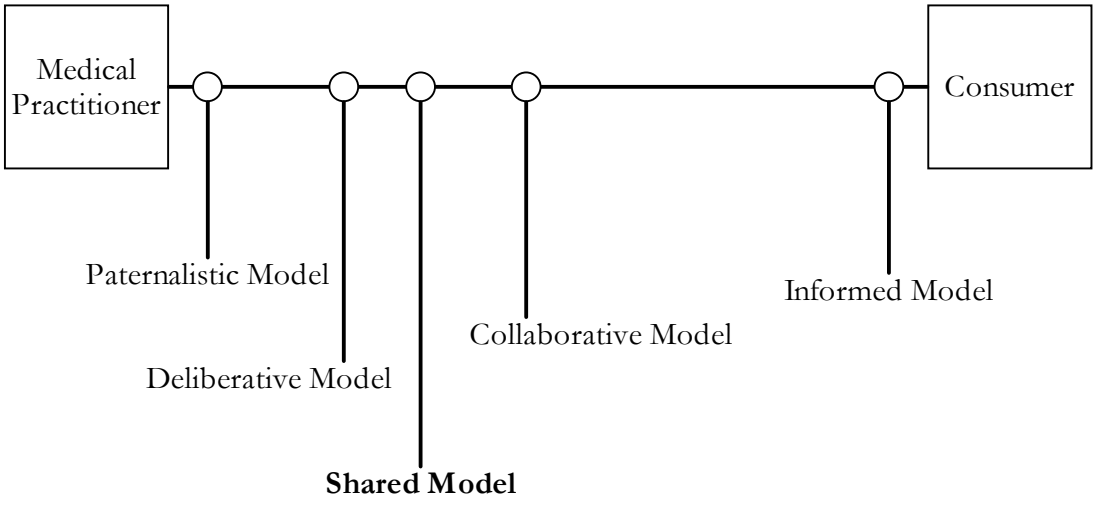

Figure 6-6 Medical practitioner/consumer decision-making models described by Emanuel and Emanuel (1992). Charavell et al. (2001) add an additional model, the 'shared decision-making model'

The results from this work described in section 5.3.4.2 suggest another expansion of this set of decision-making models. The additional models are: a consumer only decision-making model; and a model where the consumers and medical practitioners are partners in decision-making which have been illustrated in Figure 6-7.

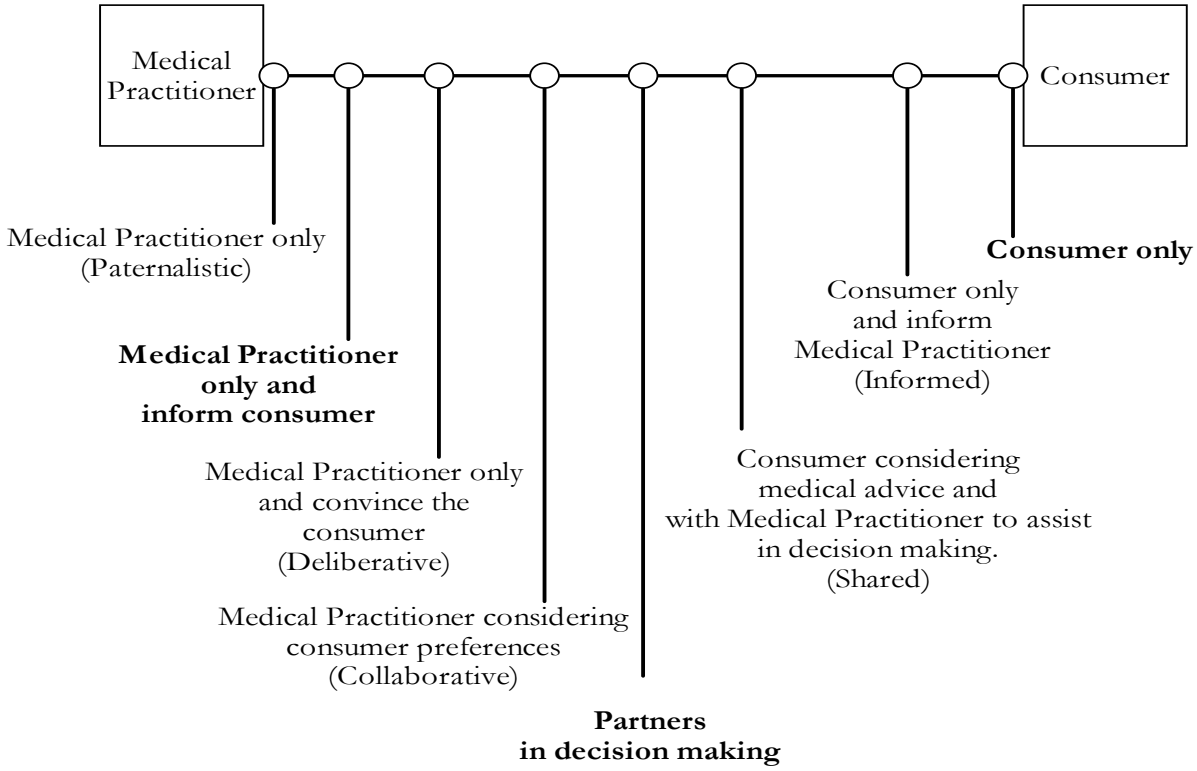

Figure 6-7 Medical practitioner/consumer decision-making models described by Emanuel and Emanuel (1992). Additions to this model include 'medical practitioner only but inform consumer', 'consumer only decision-making', and 'consumers as decision-making partners with medical practitioner'

These models have been defined as follows:

- **Consumer only decision-making** is defined as a model where by the consumers make independent medical decisions without discussion with a medical practitioner. An example of this model was in James case, where James and his wife diagnosed two ADRs; the first to Panadeine Forte, and the second to tramadol hydrochloride. The experts who reviewed this case study agreed with James' diagnosis supporting the notion that not only did he make this diagnosis, but that the diagnosis was accurate.

- **Partners in decision-making** is defined as a model where by the consumer and medical practitioner are partners in medical decision-making. This model parallels the model of

decision-making that is likely to be used between two colleagues of equal standing, but who contribute different perspectives to a decision domain. An example of this model was in Joanna's case, where Dr Carey and Joanna jointly made decisions about the management of her suspected ADR to Celebrex. In this case, Joanna contributed knowledge of the past history of the case and her analysis and reasoning to date. Dr Carey contributed medical knowledge and access to medical resources and some additional medical reasoning.

Scott and Lenert (2000) stated that they do not believe consumers are capable of shared medical decision-making because they have limitations such as education, numeracy, problem solving and understanding their own preferences. Charavell et al. (2001) stated that medical practitioners have information that consumers do not have, and that it is not until all of the information has been conveyed and the risks and benefits have been weighed that a consumer can contribute to the decision-making process.

The results of this work suggest that although medical practitioners have access to medical information and diagnostic expertise that needs to be considered prior to making a medical decision, consumers also have information that needs to be considered and discussed prior to making ADR decisions, and that both sets of information are equally important when attempting to make an ADR diagnosis. A key point, however, is that whether authors believe consumers are capable of making medical decisions is a different issue to whether they are actually making them. As stated previously, the original work by Emanuel and Emanuel (1992) uses descriptive decision theory, describing decision-making styles that are currently being used, not whether they should be used. The data from this work suggests that some consumers do make independent medical decisions, and they do participate in partnership with their medical practitioners. It can then be decided that consumer's 'should not' participate in these types of decisions because of their limitations, or it can be realised that some consumers do participate in these types of decisions, and so working together with these consumers to enhance their participation is likely to enhance medical decision-making rather than detract from its effectiveness.

One further expansion of the original model by Emanuel and Emanuel (1992) is to suggest an expansion to the Paternalistic model. According to Emanuel and Emanuel (1992) the

Paternalistic decision model is defined as a model where by the clinician has complete authority to make decisions on behalf of the consumer. This model may include:

- **decisions made by the medical practitioner without informing the consumer**, such as which anaesthetic drugs to use during surgery;
- **decisions made by the medical practitioner where the medical practitioner informs the consumer of the decision that has been made**, such as a change to a surgical procedure that happened during surgery, based on what was found at the time of surgery.

Another dimension to these models is the consideration of matching the decision model used by each of the decision-makers. In the case study of Paul, Dr Kent used Charavell et al.'s (2001)'s shared decision-making model. Dr Kent's expectation was that he would provide information and Paul would make his own decisions. Paul, however, expected and wanted to be using a collaborative model, where the medical practitioner would make the decisions having discussed the issues surrounding the decision with Paul. The result of the mismatch between the models each decision-maker expected to use contributed to a breakdown in the medical practitioner/consumer relationship. The implication of this is that a discussion between decision-makers about the preferred model of decision-making may assist with this problem.

A final dimension to these models is that different circumstances allow or require different decision models. Clearly decisions made within surgery cannot be made in conjunction with the consumer at the time of decision-making. A plan can be made between the decision-makers prior to surgery, but in some cases the plan will need to be changed according to the circumstances, especially in emergency situations. Similarly, decisions about when to seek medical assistance, and which medical practitioner to consult, fall clearly in the domain of consumer only decision-making. The more complex the medical situation and the more time constrained the decisions are, the more likely the decision model most appropriate to the situation will move towards the medical practitioner's end. Decisions that are more the right and responsibility of the consumer that require skills that are used outside the decision domain, such as logic and reasoning, the more likely the most appropriate decision model will be to the consumer end. It is the models in the middle that are likely to be preference related, and therefore require negotiation between decision-makers.

There is significant discussion in the literature about the role consumers are capable of taking, and want to be taking. These data support the notion that consumers are all individuals, and different consumers have different abilities to participate in the medical decision domain, and different levels of interest in taking responsibility for their health care. With the movement towards evidence based practice, considering consumer's contribution to medical decision-making is important. Considering the impact of excluding the consumer's contribution is also important. The additional models suggested from this work indicate that the role consumers currently take in medical decision-making is broader than is being described in the literature, and the acknowledgement of that, and the recognition that individual consumers have differing needs is an important factor to be taken into account when making ADR decisions.

6.3.3. ADR DIFFERENTIAL DIAGNOSIS

The results of this work revealed a number of strategies used by the participants, including the consumers and medical practitioners, when making a differential diagnosis. Figure 6-8 is a model of the strategies used.

This model illustrates some of the complexities surrounding the diagnosis of an ADR. The key concepts within the model are diagnoses, symptoms and drugs. Each of these concepts has a list of characteristics listed below.

Characteristics of diagnoses

- Considering a set of possible diagnoses.
- Matching a set of symptoms to the most likely diagnosis/diagnoses.
- Gathering information to support or eliminate each diagnosis. Information may:
    - be purposefully gathered (asking questions, ordering tests);
    - appear over time (multiple incidences of a suspected ADR, progression of a condition or disease).
- Holding one or more possible diagnoses at any one time.

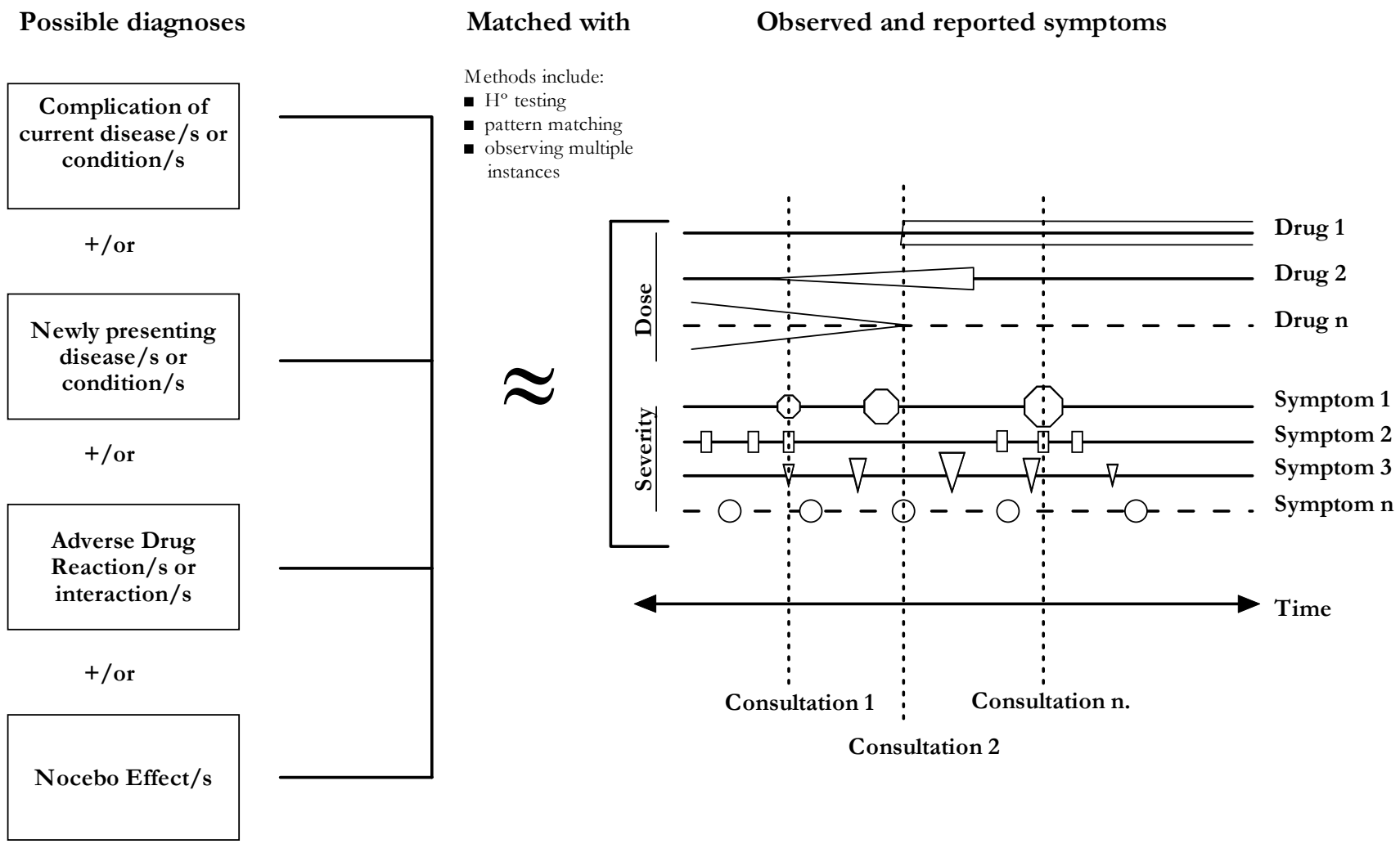

Figure 6-8 An emerging model of differential diagnosis

Characteristics of symptoms

- Symptoms can start and stop along the timeline.
- Symptoms can increase or decrease in severity.
- Symptoms can be: observed by medical practitioner; reported by a consumer or family member, or come from test results.

Characteristics of drugs

- Drugs can be started and stopped.
- Drugs have a dosage which can change over time. The dosage may be increased, decreased or remain static.
- The number of drugs a consumer is taking at any time can be from none to multiple.
- The drug may have been prescribed by the medical practitioner, another medical practitioner or self-medicated (non prescription).
- The drug may be a prescription drug, an over the counter drug or a complementary medicine.
- The medical practitioner may know about all or none of the drugs the consumer is taking at any time.

As well as including individual concepts, this model illustrates some relationships between these concepts:

- A set of symptoms may be as a result of one or more possible diagnoses (some symptoms associated with one diagnosis and other symptoms associated with a different diagnosis).
- Multiple symptoms may result in a single diagnosis.

Figure 6-8 attempts to illustrate these emerging differential diagnostic processes, whilst highlighting the complexity of this decision type. This figure has four potential diagnoses down the left side: a complication of one or more pre-existing diseases or conditions; one or more newly presenting diseases or conditions; an adverse drug reaction or interaction; or a nocebo effect. One or more of these possible hypotheses is matched with a set of symptoms. The methods of matching the diagnoses with the symptoms included hypothesis testing, pattern matching or observing multiple instances of the same set of symptoms. The section on the right of this figure, illustrates the complexities of symptoms and drugs. Drugs are commenced and

ceased at various times within a person's life. The dosage may be stable, increasing or decreasing at any moment in time. The symptoms may be increasing, decreasing, intermittent or stable. Knowledge of symptoms and drugs, therefore, requires an understanding, not only of what is presented at the time, but also the history of their progression.

The process of differential diagnosis, according to this emerging theory, is the matching of one or more symptoms or patterns of symptoms (observed or reported) to one or more possible diagnoses, and determining the diagnosis that is most likely to explain the set of symptoms at any point in time.

This model of ADR decision-making is an amalgam of decision-making strategies articulated by multiple participants. No single participant used all of the strategies within this model, however it appears that thorough diagnosis would include each of these strategies, and therefore the model illustrates a prescribed decision-making process which was derived from descriptions of ADR decision-making, and description of when ADR decision-making was ineffective, or less than effective.

Table 6-5 highlights some of the differences observed between the strategies used by consumers compared with those used by the medical practitioners when making ADR diagnostic decisions.

Medical practitioner diagnostic strategies	**Consumer diagnostic strategies**
Hold multiple hypotheses	Work with a single hypothesis at a time
Aware of a range of possible diseases or conditions	Searching for any possible diseases or conditions that may account for symptoms
May have seen the symptoms and/or condition in other consumers, self, family or friends.	May have seen the symptoms and/or condition in self, family or friends.

Table 6-5 Differences between consumers and medical practitioners in diagnostic strategies

The ADR differential diagnostic strategies that have emerged from the case study data, individually are not new. The methods of selecting an option from a set of hypotheses and pattern matching (described in section 2.3.5.2) fit with Elstein and Schwarz's (2002) descriptions of hypothetic deductive reasoning and pattern matching. The idea that different methods are

used by different decision-makers depending on the circumstances of the decision was reviewed in section 2.3.5.2 and was described by O'Neill et al., (2005).

Other methods of ADR diagnosis have included strategies for a single rather than multiple decision-makers, and have used hypothetico-deductive rule based methods rather than including the role of pattern matching in this form of diagnosis, (American Society of Consultant Pharmacists, 1998; American Society of Health-System Pharmacists, 1995; Naranjo et al., 1992; VDUAC, 1999; WHO, 2002). Also these methods have included the differential diagnosis between an ADR and a disease or condition, but have not included the hypothesis of a nocebo.

The implication for a decision support system designed to support differential diagnostic decisions, therefore, would be the use of a combination of theories, for multiple decision-makers and the inclusion of the four possible hypotheses rather than two or three that are usually considered. The following sections revisit the decision theories described in chapter two, that might be useful in developing a decision support system of this type.

6.3.3.1. Utility Theory

Utility Theory was described in section 2.3.5.3. The decision-makers in case studies presented in chapter four, appeared to be holding one or more hypotheses at any point in time, and were adjusting the weights of each hypothesis. At any point in time, a series of hypotheses were being considered, and each had a weighting or likelihood attached to it. Information was gathered to support or eliminate each hypothesis, and as new evidence was presented or gathered, the weightings changed. The medical practitioner's did not make definite statements about which was the 'correct' hypothesis, just which hypothesis was most likely.

In Toni's case, the hypothesis with the highest weighting was a "flu like virus". After Toni presented a second time, with a newly presenting symptom of a rash, "that looked like an allergy", Dr Barns added an additional hypothesis to the list of possible hypotheses, an ADR, and increased its weight compared with the weight of the virus. After obtaining the test results, and a discussion with the specialist, it appears the hypothesis of a virus had a lowered weighting and the weighting of an allergic reaction to the Tegretol increased. Dr Barns said "Sometimes you are really guessing. You are saying what's more likely, rather than really being certain."

6.3.3.2. Case-based reasoning for familiar diagnoses

Case-based reasoning, discussed in section 2.3.5.5, is a method of solving new problems by accessing a database of old problems. The medical practitioners referred to past cases within their own experience that assisted in making decisions about the case in question. An advantage of case-based reasoning is that rather than only using cases within a person's own experience, cases can be stored in a database and shared with other decision-makers. This method can be used in several ways to assist with diagnosis:

- Cases can be collected and stored so that decision-makers can find similar cases to assist in making a diagnosis that may be novel to this decision-maker, but is not novel to a group of decision-makers.
- Cases can be used to either support a diagnosis or eliminate a diagnosis.
- Cases can be combined to form a 'typical' case that can then be used as 'best practice'.

In some situations, the medical practitioners within this work referred to past cases they had experienced which either added additional weight to a particular hypothesis, or lowered the weighting of a particular hypothesis. Dr James said that he has seen similar cases of drug induced lupus associated with hydralazine. In these past cases, the dosage of the medication was significantly higher than in Irene's case. This case was similar to past cases, which appeared to bring the past cases into consciousness for consideration. This case, however, had a key difference to the past cases, the difference in dosage, which appeared to reduce the weighting Dr James placed on this hypothesis. The other hypothesis Dr James appeared to be holding was that the symptoms were as a result of a Nocebo effect, based on Irene's past history of multiple suspected ADRs, which it appears, Dr James believed were partially due to a Nocebo effect. This appears to be a second use of case-based reasoning, considering this diagnosis against the results of past diagnoses for this particular consumer.

6.3.3.3. Cognitive theory for novel diagnoses

Another aspect of ADR decision-making appeared to be related to a more cognitively driven decision-making process, where the decision-maker actively seeks and tests one or more hypotheses. This appeared to be the process when the medical practitioner did not have a past

case that matched the current case providing a clear initial hypothesis, indicating the diagnosis was a novel, or unfamiliar diagnosis.

It did not appear that any of the decision-makers began with all four types of hypotheses indicated in Figure 6-8 at the beginning of the decision-making process. It appears that they began with one or two possible hypotheses, and only introduced a new hypothesis if something about the condition changed, resulting in the need to reconsider the possible hypotheses. This may have been because: a treatment did not work, as in Paul's case; the condition did not progress as expected based on the first hypotheses, as in Toni's case; the hypothesis was challenged by another decision-maker as in Mary's case; or new symptoms appeared as in Toni's case.

A single decision strategy, therefore, does not appear to account for the multiple facets of decision-making in this small but complex domain. Multiple decision strategies appear to be being used at different stages of the decision-making process, indicating the need for multiple theories to underpin the development of a decision support solution within this domain.

6.3.3.4. Idiosyncratic characteristics of ADR diagnoses

ADR diagnostic decision-making appears to be different to traditional medical decision-making, as consumers untrained in medicine have made diagnostic decisions that have been supported by ADR experts. This provides additional insight into this decision domain.

In cases where there was a clear temporal link between the commencement of the drug and the onset of the symptoms, with no other concurrent conditions or diseases, the diagnosis required only observation, logic and reasoning. In this set of cases, medical knowledge was not required. Medical knowledge would have allowed the decision-maker to eliminate other possible diseases that could also have resulted in a similar set of symptoms, but was not required to suspect an ADR.

The diagnosis becomes more complex with multiple factors:

- multiple drugs;
- multiple conditions;
- multiple symptoms.

In cases where there was a newly presenting condition or disease, the diagnosis was complicated by determining which symptoms were associated with the drug, and which symptoms were associated with the other condition or disease. In Paul's case, Dr Kent believed that some symptoms were associated with the drug, and some symptoms were associated with a newly developing disease.

In cases where there were multiple conditions and multiple drugs, sorting out which symptoms are associated with which hypothesis is difficult, and knowledge of diseases and the patterns of symptoms associated with those diseases is important when making this type of diagnosis.

It appears, therefore, the consumers in this work made ADR diagnoses in situations where medical knowledge is not required. They also appeared to be able to make diagnoses with some limited medical knowledge based on their own investigations or experience.

6.3.3.5. The nocebo effect as a possible hypothesis

When attempting to differentially diagnose an ADR from a pre-existing or newly developing disease, one hypothesis in Figure 6-8 was that the symptoms were caused by a nocebo effect, or negative placebo effect.

Within this work, no clear set of strategies emerged for differentially diagnosing between a nocebo effect and some other possible explanation of the symptoms. Two possible strategies did emerge: if the symptoms are not symptoms known to be associated with the drug or set of drugs suspected, and no other cause can be found, it may be a nocebo effect; or if the consumer is a person who appears anxious about taking medications and is what the medical practitioners consider overly anxious about the possibility of experiencing an ADR, the symptoms are more likely to be a nocebo effect.

The difficulty with the first strategy relates to the complexity of developing knowledge of previously undocumented ADRs. If no explanation for the symptoms is found and so the medical practitioner assumes the symptoms to be associated with a nocebo effect, it will not be reported to ADRAC. Symptoms that have not previously been associated with a particular

medication, and no other possible diagnosis has been found, may be a previously undocumented ADR associated with the medication, and unless medical practitioners report this type of case, this knowledge will not be added to the developing body of ADR knowledge.

The difficulty with the second strategy is that the person who is anxious and very focused on the possible ADRs associated with medications, may be a person who has experienced many ADRs and has developed a fear, or has a particular 'sensitivity' to medications, as described by the experts, which may mean they are more likely to experience ADRs to medications. No clear strategy in determining which explanation is most likely emerged from this study.

Another complexity of the nocebo effect, is that the symptoms medical practitioners sometime believe are the results of a nocebo effect, are symptoms known to be associated with a particular drug, and the belief is that because the consumer is aware that this set of symptoms may be associated with a particular drug, it is these symptoms they develop as a nocebo effect. It is not clear from the case studies how a medical practitioner can make a differential diagnosis between a set of symptoms known to be associated with a drug which are caused by a drug, and which are caused by a nocebo effect.

An article by Barsky et al. (2002), discusses the issue of the nocebo phenomenon associated with medications. They categorise two sets of symptoms " 'specific side effects' are symptoms or physiological changes that result directly from the specific biological and pharmacological activity of the drug and tend to be dose-dependent and predictable." This definition is the equivalent of the Type A reactions described in section 2.2.4.1. The second set of symptoms they describe as " 'non-specific side effects' are symptoms or physiological changes that cannot be explained on the basis of the known pharmacology of the drug and are idiosyncratic and not dose dependent. In theory non-specific side effects may be positive and beneficial or negative and adverse." Type B reactions are uncommon and independent of a drug's known pharmacological properties. They are considered the most serious and are potentially life threatening (Kalachnik, 1999). The 'non-specific side effects' described by Barsky et al. (2002) fit with the definition of a Type B reaction, except for the expected level of severity. Barsky et al.'s (2002) definition includes milder symptoms were as the Type B definition describes serious reactions.

Barsky et al. (2002) argue that the 'non-specific side effects' may be largely accounted for by the nocebo effect. When a drug trial occurs, one control group receive the drug and the control group receive a placebo. Barsky et al. (2002) highlight the high incidence of ADRs reported by participants receiving the placebo, which they attribute to the nocebo effect.

Publication of this paper resulted in several letters to the editor in response. Within these letters an issue was raised that a placebo is a compound. It is possible that a consumer has had a reaction to the compound used within the placebo drug (Golomb, 2002). Another respondent (Caspi, 2002) suggested future work incorporate:

> …a 2 x 2 matrix comprising four conditions in which subjects are (1) told they will get a drug and receive a drug, (2) told they will get a drug but receive a placebo, (3) told they will not get a drug but receive the drug in a disguised form, and (4) told they will not get a drug and receive a drug (p. 2502).

In response to the letters, Barsky et al. (2002) concede "…in clinical practice, however, this distinction may be all but impossible to make".

The danger in not identifying a nocebo effect is that drugs are attributed with ADRs incorrectly, limiting the use of a potentially useful therapeutic tool. The danger in incorrectly diagnosing symptoms as a nocebo effect is that the consumer experiencing the symptoms may be diagnosed incorrectly.

One case study within this work that illustrates the problem is Irene's case. Without explicitly stating his reasoning, Dr James appeared to be suggesting that some of Irene's symptoms were a nocebo effect rather than effects of the drugs based on behaviours that did not appear logical to him. Irene fits the personality characteristics described by Barsky et al. (2002), and it is possible that this is the case.

It is also possible that Irene's anxiety and focus on her health is based on a fear that has evolved having experienced multiple ADR due to an underlying metabolic condition that has not been

diagnosed, as suggested by one of the experts. Diagnosing a nocebo when there is an underlying condition is clearly not a diagnosis that most serves the consumer. Diagnosing ADRs that are actually the result of a nocebo effect also have negative connotations.

A key implication here is that further research is required to understand this phenomenon more clearly to assist in the process of differentially diagnosing ADRs.

6.3.4. THE ROLE OF THE CONSUMER IN THE ADR DECISION DOMAIN

In chapter two, a table (Table 2.3) was presented that illustrated the decision-makers in the ADR decision domain, and the types of decisions each decision-maker participates in. This table was derived from the literature, the preliminary background work to this thesis, and analysis of the current ADR decision support systems designed to assist decision-makers with ADR decision-making. This table has been included again, below, to remind the reader of its content. Table 6-6 includes the primary decision-makers within the ADR domain, and the decision types within the ADR decision domain that were identified through the literature and the preliminary background studies. As can be seen from this table, the medical practitioner makes the majority of the decisions within this environment, with the lower case indicating a partial role. The consumers, therefore, participate in the treatment decisions and make decisions about life style and when to seek treatment. The diagnostic decisions are the domain of the medical practitioners with the ADR experts, and the information supplied by ADRAC, assisting in this process.

	Consumer	Medical Practitioner	ADR Expert	Pharmacist
Detecting and Diagnosing		X	X	
Treatment	x	X		
Prescribing		X		
Reporting	x	X		X
Seek treatment (Broadstock & Michie, 2000)	X			X
Lifestyle decisions (Broadstock & Michie, 2000)	X			X

Table 6-6 Decision types made by each decision-maker

The results presented in chapters four and five suggest that in the area of ADRs, consumers make decisions that are broader than those illustrated in Table 6-6.

6.3.4.1. Consumers as ADR diagnostic decision-makers

The results from the work of this thesis indicate that the consumers in this study not only detected their suspected ADRs, but in many cases their suspicions were confirmed by the experts, strengthening the argument that these consumers had the ability to recognise a set of symptoms as being likely to be associated with a drug rather than symptoms of either a pre-existing disease or a newly developing disease, a process referred to in the medical community as differential diagnosis.

Table 6-7 illustrates the additional consumer decisions illustrated by this work. The sections in an font that is not bolded, indicate the decision types made by each decision-maker that were previously known, and the bolded sections represent the decision types made by each decision-maker that were found in this work.

	Consumer	**Medical Practitioner**	**ADR Expert**	**Pharmacist**
Detecting and Diagnosing	**X**	X	X	
Treatment	X	X		
Prescribing		X		
Reporting	**X**	X		X
Information sharing	**X**			**X**
Information seeking	**X**			**X**
Lifestyle decisions (Broadstock & Michie, 2000)	X			X

Table 6-7 Consumer role in ADR decision-making

As can be seen from Table 6-7, the decision types made by the consumer include diagnostic decision, treatment decisions, information seeking and information sharing. The decision type of information sharing is an additional decision type that emerged from these data.

When combining the discussion of the medical practitioner/consumer decision models in section 5.5.1.2, the discussion of ADR diagnostic decision-making in section 5.2.2.2, the results that discussed the strategies consumers used to make ADR diagnostic decisions, and the various decision types discussed in this chapter, there is mounting evidence of the role consumers play in ADR diagnosis. Not only did consumers make ADR diagnostic decisions within this work, and were capable of making those decisions, a set of strategies also emerged illustrating how they did it.

6.3.5. ADR DECISION-MAKING BASED ON PARTIAL KNOWLEDGE WHICH CONTRIBUTES TO THE INCIDENCE OF ADRS.

The results that informed partial knowledge came only from the analysis of the single case studies. It was this level of analysis, where multiple views of a single instance of an ADR, that the differences in understanding, at an individual level, were most apparent. These results suggest that ADR knowledge is distributed between multiple decision-makers and each decision-maker has access to some knowledge unknown to the other decision-makers and some that is shared between decision-makers.

Figure 6-9 illustrates knowledge within the ADR decision domain and the relative proportion each decision-maker has to each of the three sources of knowledge. The three sources of knowledge include: knowledge of drugs and drug behaviour; knowledge of diseases and conditions; and knowledge of consumer behaviour and the consumer medical history (recorded history and unrecorded history).

It appears from this work, that most ADR decisions are made with only partial knowledge. This work illustrated some problems that arose in the decision domain which appeared to result from decision-making with partial knowledge. Partial knowledge has several dimensions. It may include:

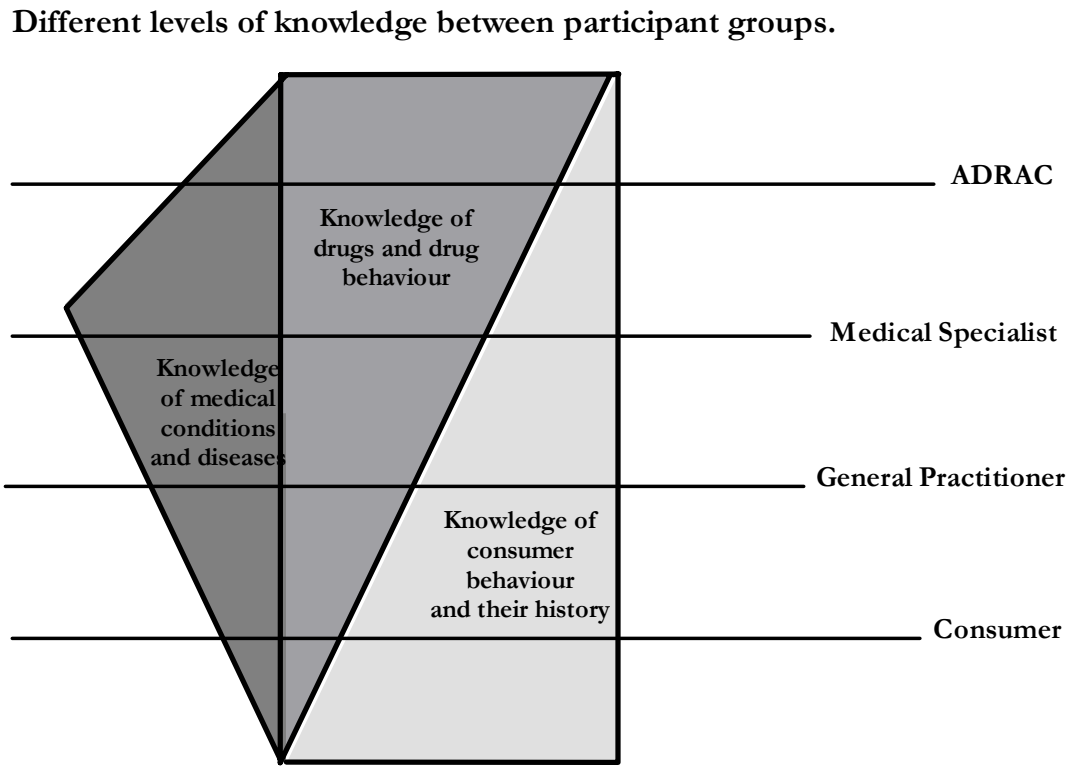

Figure 6-9 Knowledge in the ADR decision domain

- access to only some of the available ADR knowledge:
    - consumers with limited knowledge of potential ADRs to drugs;
    - consumers with limited knowledge of the likely progression of ADRs;
    - consumer's awareness of the risks of a drug compared with the benefits of the treatment and the risks of not treating the disease. This result has been discussed in detail in a recent health informatics conference paper (O'Brien & Yearwood, 2004);
    - medical practitioners unable to keep up-to-date with the large number of drugs that are introduced into the market place;
    - different decision-makers placed emphasis on different knowledge sources, resulting in different preferred decisions.

- partial awareness of the completeness of the knowledge used in ADR decision-making is at any point in time (That is, partial awareness of what knowledge exists that the decision-maker is not aware of):

    - medical practitioner's awareness of the consumer case history;
    - medical practitioner's awareness of the consumer's concerns, fears, perceptions, impact of an ADR;
    - medical practitioners limited knowledge of all available knowledge about potential and preventable ADRs;
    - consumer's awareness of the reliability of the information s/he accesses;

- knowledge of one definition or understanding of a concept and lack of knowledge or understanding of the other perspectives of ADR concepts:

    - consumers labelling a set of symptoms, for example, as an 'allergy' (using a term to mean 'symptoms associated with a drug', and the medical practitioner saying it is not an 'allergy', meaning 'it is another type of ADR, but not an allergy';
    - the consumer's level of concern compared with the medical practitioner's awareness of the consumer's level of concern.

The impact of partial knowledge in the ADR decision-making domain included:

- consumers making decisions based on incomplete knowledge. An example was Helen was not aware that her pre-existing condition may cause severe pain, and so did not purchase pain killers. In the middle of the night, the only pain killers in the house were Panadeine Forte prescribed for her husband, and so she chose to take that medication;
- a break down in trust between the consumers and medical practitioners;
- prescribing a drug for a consumer that was contra-indicated according to the experts
- a lack of diagnosis:
    - leaving the consumer open to experiencing a second ADR from the same drug resulting in frustration of symptoms that have no diagnosis.

The implications of this emerging theory, is that if partial knowledge does contribute to the incidence of ADRs, and the ability to detect and manage them quickly, roles for ADR decision support may be to assist in:

- storing all this information centrally, a solution that has been a focus of centralised medical records;
- facilitating sharing of this information between decision-makers;
- accessing relevant information from within complex computerised medical records, and bringing this information to the attention of the decision-makers.

Intelligent software agents (ISA) described in chapter two, have the ability to perform functions such as these. Limitations at this stage are that most medical records at this stage are still paper based, and electronic records are central to a medical service rather than centralised for a consumer. This technology may be useful in the future when the sharing of electronic medical data is established.

6.3.6. PROBLEMS WITH GENERATING NEW ADR KNOWLEDGE

The final set of results emerging from the case studies relates to developing new ADR knowledge. As described in the introductory chapter, the TGA is the central body in Australia for collecting reports about potential ADRs. A figure that has been used extensively when discussing this work has been included below (Figure 6-10).

As can be seen from this figure, the process of developing new ADR information is via reports from consumers and medical practitioners. These reports are reviewed by ADRAC and are stored in the ADRAC database.

Within the case studies, the medical practitioners and consumers used existing knowledge to make decisions about suspected ADRs. If they could not locate information about a suspected ADR, they were more likely to decide that the drug and symptoms were not related. That is, they used current knowledge of ADRs to inform the process of differential diagnosis. The idea that the medical practitioners were diagnosing a set of symptoms that may be a previously undiagnosed ADR did not appear to be a factor considered in most cases. The hypothesis that

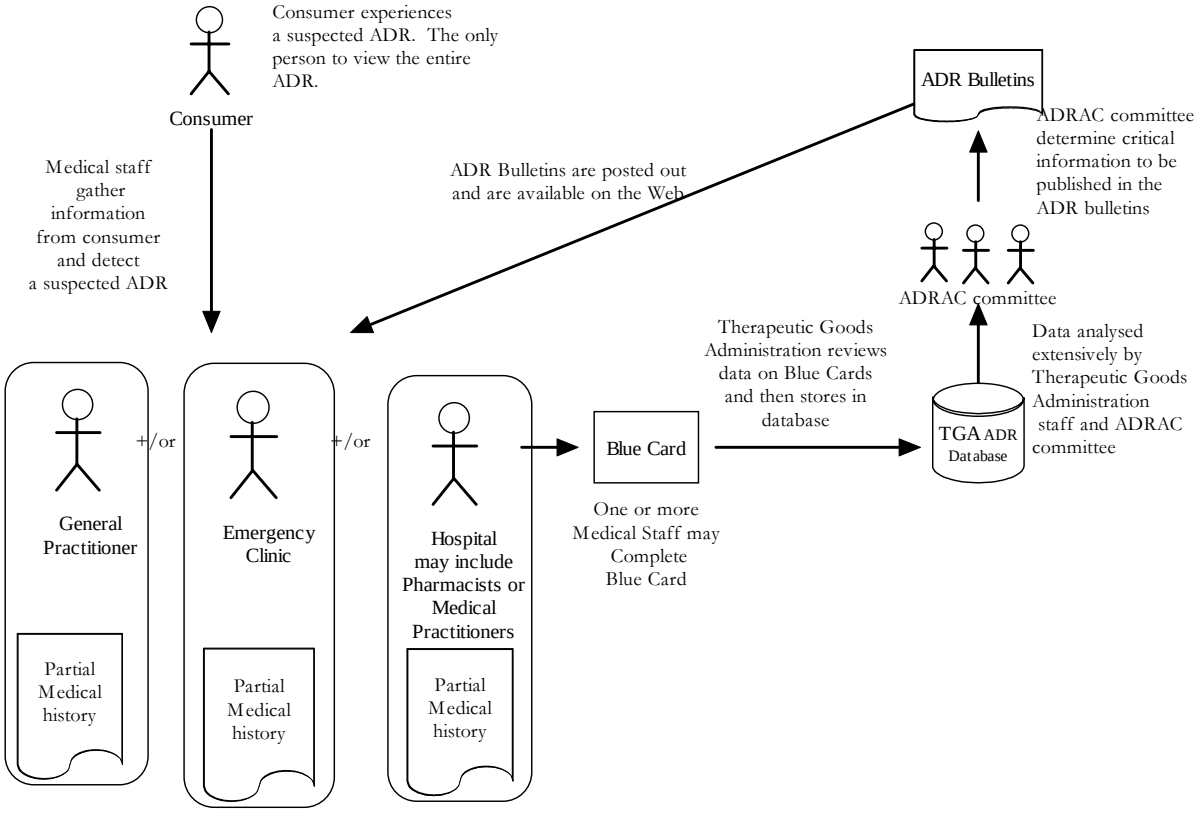

Figure 6-10 Collection and dissemination of ADR information by ADRAC

the symptoms were a nocebo, or belonged to a pre-existing or newly developing disease appeared to be a more likely diagnosis, in their minds.

None of the medical practitioners nor consumers in this work reported the suspected ADR. Three reasons were given by the medical practitioners: it is a known ADR as is well documented; it is unlikely to be an ADR; the reporting processes are too complex. Although consumer reporting has been available in Australia for many years, it has not been promoted and a dedicated consumer reporting service has only been introduced within the past year. The data collected for this work occurred prior to the promotion of this service.

The preliminary background studies (O'Brien & Yearwood, 2002, 2004), found that the number of reports sent to the TGA are likely to be significantly lower than the number of suspected

ADRs that occur. One reason for this is because the TGA promotes the reporting of serious or unexpected reactions to new drugs.

Of the three reasons, the ADRs that are known and have been well documented, did not need to be reported. The other two groups, however, would have assisted in developing the ADRAC database.

The paradox of this situation is that the medical practitioners and consumers rely heavily on what is currently known about ADRs, but unless they report cases where: the suspected ADR was unknown to them, or there is a variation in this particular case compared with what they previously knew about this type of case; or they believe there is unlikely to be a relationship between the suspected drug and the newly presenting symptoms, but there is some doubt; this knowledge, which decision-makers in this domain depend on, will remain out of date.

Another problem that emerged from these case studies, was that even when an ADR was described by a medical practitioner as 'known', the medical practitioner did not recognise it as an ADR within the clinical setting. This indicates that perhaps documenting 'unknown' ADRs is not enough, and that the medical practitioners may benefit from a decision support system that assists in recognising ADRs, regardless of whether they are known or not.

The decision support systems described in chapter two, used within a hospital setting to alert hospital staff that a consumer may be experiencing an ADR, used rule-based engines to recognise a subset of possible ADRs. This issue suggests that medical practitioners and consumers within a community setting may benefit from technology that performs a similar function. As the context is different, the system would need to work differently. These hospital based systems used information that was available in their centralised electronic hospital medical record. The medical records in the community settings at this stage are still primarily paper based, and may be stored by multiple medical practitioners in multiple locations.

The results relating the development of new ADR knowledge, however, highlight the importance of resolving the problems of non-reporting, and suggest that documenting

knowledge about ADRs is not enough, and that decision support may have a role in detecting suspected ADRs.

6.4. Evaluation of the research process

The results that have emerged from these case study data that were documented in chapters four and five, have added to current knowledge of the ADR decision domain. These contributions, however, have some limitations. Some limitations of the methodology were discussed in chapter three. The implications of those limitations are discussed below.

6.4.1. IN-DEPTH ANALYSIS OF FIFTEEN CASE STUDIES

Fifteen case studies are unlikely to be representative of the population of ADR case studies. The result of this thesis, therefore cannot be generalised to the wider ADR population. This work is exploratory in nature, and so generalising the results was not a goal. A large amount of data were generated from this small group of case studies, and an advantage of using this smaller number was that very in-depth analysis could be performed. The emerging theories have been imbedded in the data and can be tested using qualitative research methodologies to determine the extent that they can be generalised. Exploratory work is a necessary stage so that new ideas can emerge, which can then later be tested to determine the degree that they are present in the wider population.

6.4.2. CONSUMER VOLUNTEERS

The consumers and experts were volunteers and so as a consequence are likely not to be representative of all consumers, and all experts. The medical practitioners were not volunteers, but from the group that were targeted, those that agreed to participate did self select. The 30% of medical practitioners who declined may have had a particular set of characteristics.

When the cases were viewed there was significant stratification of the data, providing insight into a wide variety of case types, (refer to Table 4-2). All except for Type C reactions were represented within this group of case studies. It is not known if the distribution is typical of the population of ADR case studies.

The use of volunteers has similar implication to a small sample size. Generalisation cannot be made, and awareness that some attributes of the participants may not be typical of all participants, is necessary when interpreting the results.

Although a significant proportion of the consumers in this study were involved in diagnostic decision-making, not all consumers are. The implication, therefore, is not that all consumers have the ability to, and/or interest in participating in ADR diagnostic decisions, however, this work shows that some are capable and interested. It is not known what proportion of all consumers this relates to, but it means that this group of consumers need to be recognised within this domain.

6.4.3. CHOICE OF PARTICIPANTS

Consumers, medical practitioners and experts were the only participants who were interviewed. The data suggested that other decision-makers in this domain included pharmacists, the consumer's family and friends and other health professionals. An analysis of the roles these other decision-makers in this domain play, in particular the role of the pharmacist, and the role of the family and friends, may add additional insight not revealed by interviewing only the consumers, medical practitioners and experts. The initial three, however, was a useful starting point.

6.4.4. BIAS OF THE RESEARCHERS

As was discussed in the introductory chapter, the use of the terms 'consumer' and 'medical practitioner' rather than 'doctor' and 'patient', reflect our bias towards the notion that consumers and medical practitioners each have a perspective that is important within any medical consultation. It is also our expectation, based on a symbolic interactionist theoretical framework, that as well as each of the participants having a perspective based on the social grouping/s they belong to, the researchers within this work also have expectations. Our biases come from our own experience as consumers, a belief that consumers are a valued member of the medical team, and experience from allied health which has a focus on family centred practice.

Grounded theory, as a methodology, is based on an assumption that researchers are able to set aside their pre-existing ideas and allow ideas to emerge from the data. It is recognised coming from a social constructionist epistemology, that this is a theoretically ideal position, one that cannot humanly be adhered to completely. As an ideal, however, it allows researchers to become aware of their own pre-existing ideas, to acknowledge them, and then attempt to be open to newly emerging ideas. The use of using grounded theory revealed some results from the data that were in line with the preliminary thinking of the researchers, and other results that were not expected, and challenged the preliminary thinking. The use of this methodology, therefore, was a useful tool to assist in understanding newly emerging themes from the data.

The theories that have emerged from this work, which attempt to make sense of the results, are based on the results of the data combined with the perspectives of the researchers. The researchers, like the consumers, medical practitioners and experts, also construct meaning based on their preliminary understanding of the world. This is an expected result of the research process. Another set of researchers, conducting this study, are likely to view the results from a different perspective.

6.4.5. LIMITATIONS OF THE THEORETICAL PERSPECTIVE

Social constructionism and symbolic interactionism take a non-critical perspective. The aim is that all views are equally valid and they provide an avenue to observing rather than taking a critical stance. These theoretical perspectives, therefore, are not sensitive to issues of power between groups. The use of first names for consumers and the title Dr. for each of the medical practitioners, reflects the researcher's awareness of this hierarchy within the social systems this work was conducted within. The dominance of the medical view in the decision making was reflected: within the data; within the pre-existing medical practitioner/consumer decision making models; and within the current focus of decision support within medicine. The use of symbolic interactionism, as a theoretical framework, did not highlight these issues explicitly. To highlight these issues a critical methodology would have been required.

The research questions within this work were about the perspectives of each decision-maker and their contribution to ADR decision-making. Although the power issues would have added an additional dimension to this work, they were not fundamental to the questions being asked.

6.5. Conclusion

Chapter six began with a discussion of the concepts within the ADR decision domain. Analysis of the case study data revealed that many of the concepts within this domain are multi-dimensional. That is, different groups of users had different understandings of the concepts.

The following section was a discussion of the contributions the work of this thesis made to theory. Contributions included the following:

- the use of multiple perspectives and triangulation to inform systems design;

- an expansion of Emanuel and Emanuel's (1992) medical practitioner/consumer decision models. Analysis of the case study data added two additional models to this framework: consumer only decision-making, and medical practitioners and consumers as partners in decision-making;

- insights into how ADR differential diagnosis occurs. This then can be used to determine which decision theories and technologies can be applied to this problem;

- the role of the consumer in the ADR decision domain, including consumers as diagnostic decision-makers;

- the contribution of partial knowledge to the incidence of ADRs. The consumers, medical practitioners and experts all had specific knowledge that was unknown to the other participants. Decision-making with only partial knowledge contributed to the incident of ADRs and failure to detect ADRs in some of the case studies;

The final section in this chapter is that of evaluating the research processes, discussing the limitations of this work.

CHAPTER SEVEN

Conclusion

7.1. Introduction

This concluding chapter will outline the key contributions this work has made to knowledge. This will include the contributions of the research process (7.2.1) and of the emerging theory (7.2.2). These contributions will then be discussed in relation to the implications for the prevention, detection and management of ADRs (7.2.2.1), and also the implications for the development of ADR decision support (7.2.2.2). Suggestions for future work will be discussed in section 7.3.

7.2. Contributions to knowledge

The overall aim of this thesis was to develop an understanding of the ADR decision domain to add to current knowledge of how ADR decisions are made, the problems that arise when making these decisions, the complexities and the impact ADRs have on people.

This work had three key purposes, which correspond to the contributions this work has made to knowledge:

- to add to knowledge of this domain, so that it can be used by the decision-makers to assist in the prevention, detection and management of ADRs;
- to provide an understanding of the domain that can be used to inform the requirements analysis phase of ADR decision support;
- to determine the extent that methodology used within this work can be applied to the requirements analysis phase in the field of software and/or systems engineering.

Some of the findings have been previously documented in the literature. Some outcomes, however, expand on current knowledge, and relate to the primary purposes, described above. These contributions are described below.

7.2.1. THE CONTRIBUTION OF THE RESEARCH PROCESS TO THE DEVELOPMENT OF DECISION SUPPORT

The majority of systems development begins with an assumption of who the end users are, and scoping of an intended project based on this assumption. Systems development, also, has traditionally come from a positivist theoretical framework, where the aim is to provide information systems that are based on a uniform understanding of the core concepts.

Some work has been done within the Information Systems (IS) community to move towards the use of qualitative research methods to inform the requirements analysis phase of systems engineering and to move towards the use of philosophical perspectives other than objectivism. Qualitative methodologies, including the use of grounded theory, have been used within the field of IS to analyse case studies as a tool for gathering requirements prior to the development of information systems. The concern raised by some authors has been the cost of gathering requirements using these methodologies, despite significant gains in understanding of the domain through the use of this methodology.

The work of this thesis has included a combination of a social constructionist philosophical perspective, symbolic interactionist theoretical framework and grounded theory analysis of case studies made up of multiple perspectives of a single instance of an ADR. This framework has taken the methodologies used within the IS research one step further. Qualitative methods can be used to analyse case study data, based in a positivist theoretical framework. This work, however, has used triangulation of multiple perspective case studies using a theoretical framework that embraces understanding the differences between decision-makers rather than attempting to reconcile those differences. This has added an additional dimension to current understanding of this decision domain.

The concerns over the costs of using this type of methodology within a business context are likely to be different when applying it to a decision domain within the area of consumer safety.

The costs of ADRs include the immediate costs of longer hospital stays, the treatment of the illness or injury, prescribing additional medications and lost time for the consumer in the workforce. The intangible costs are associated with loss of trust between consumers and their medical practitioners and limiting a consumer's treatment options based on a past injury or fear of future treatments. Other costs are associated with the development of decision support systems that provide only a partial solution, or that may address the goals of the initial systems design, but may not fully address the core goal of preventing and detecting ADRs.

When the knowledge of the ADR decision domain prior to, and following the work of this thesis is compared, it can be seen that this methodology has provided additional insight that can now be used as the basis for the development of decision support. As well as providing additional knowledge from the perspective of previous work within this area, the medical practitioner perspective, it has provided an integrated understanding from the perspectives of the consumer, medical practitioner and experts, with some additional understanding of the roles of other decision-makers such as the consumer family and friends, pharmacists and other health professionals.

7.2.2. CONTRIBUTIONS TO ADR KNOWLEDGE

The work has contributed to knowledge of the ADR decision domain from a number of perspectives. These areas were described in detail in chapter six, and so will be summarised below. This is then followed by the contribution this knowledge has made to understanding of the decision-makers that can be used in the prevention, detection and management of ADRs, and then how it can be used to inform ADR decision support.

7.2.2.1. Multiple understandings of the core concepts within the ADR decision domain

The core concepts within the ADR decision domain were identified. A number of these concepts, such as 'reaction', 'side effect', 'allergy', and 'significant reaction and/or side effect' were informed by the analysis of the case study data. For each of these concepts, multiple definitions emerged from the multiple perspectives within the case study data. Another group of concepts were defined using a single perspective, such as the term 'known' which came from the expert perspective. The analysis of the case studies revealed the ambiguity within the domain that arose by using a definition that came from one perspective.

The approach of identifying the specific meanings attributed to common terms within a multi-user environment revealed different understandings even though the label for the term is the same. This phenomenon is likely to exist in any multi-user environment, especially when the multiple end-users are also from multiple end user groups. The use of a social constructionist approach to identify these differences in meaning may assist in the development of any multi-user system.

7.2.2.2. Consumer's role in ADR diagnosis

A review of relevant literature revealed that medical decision-making is primarily the domain of medically trained professionals. Decision support has recently moved towards including consumers in treatment decisions. The role of diagnosis, however, has remained the domain of medical practitioners.

The results of the work of this thesis suggest that within the ADR decision domain, consumers play an important role in ADR detection. In the majority of the case studies of suspected ADRs, the consumer was the first to suspect the newly presenting symptoms were associated with a drug, and in some of the cases, the consumer made a diagnosis that was later confirmed by the medical practitioner and/or an ADR expert.

There appear to be a number of strategies the consumers used when making a differential diagnosis, which relied on the partial knowledge of the ADR decision domain that the consumers have had access to, and have not relied on the broader medical knowledge of medical practitioners.

These data do not suggest that all consumers can or would choose to be involved in ADR decision-making at this level, but it does suggest that not only are some consumers capable of making ADR diagnostic decisions, they are currently making them, with or without the support of the medical practitioners and/or decision support. These data suggest that acknowledging this ability and role, and working to support it, may assist in earlier detection of ADRs.

In many domains, it is the expert's role to make diagnostic decisions. In areas such as car and computer repairs, the consumer may take a car or computer to an expert for a diagnosis of what

is wrong. Within these fields, it is acknowledged that the consumer may also have some knowledge that will contribute to the diagnosis. Within the area of medical decision-making, however, the specialist medical knowledge required for diagnosis has remained firmly within the medical domain. The concept of determining the role of the consumer in other forms of diagnostic decision-making, and using the consumer's knowledge and expertise, may be of benefit to any domain where a diagnostic process is involved. It is likely that in some domains the consumer role is less and in other domains there is more involvement, but an awareness that the consumer may hold partial knowledge and may be an essential contributor may be important to consider.

7.2.2.3. Partial ADR knowledge

This work suggests that each of the decision-makers within the ADR decision domain have knowledge which is important when making ADR decisions; and that most ADR decisions are made with only partial knowledge. Awareness that medical decisions are often made with incomplete and uncertain knowledge is not new. The analysis of these case study data delineated the knowledge held by each of the decision-makers (Figure 6-9), and suggests, that each decision-maker has important information, that is largely unknown by the other decision-makers. It suggests that perhaps the combining of this knowledge would result in more complete knowledge, and that decision-making with the complete knowledge may result in more informed decisions than when made with less complete knowledge.

7.2.2.4. Medical practitioner/consumer decision models

A set of medical practitioner/consumer decision models was suggested by Emanuel and Emanuel in 1992. These models are descriptive models, the models that have been observed as being used within the medical practitioner/consumer decision environment rather than models that prescribe best practice. This set of models was expanded on by Charavell et al. in 2001. The analysis of these case study data suggests a further expansion of these models.

The analysis of the case studies suggested three additional models that were observed within our case study data: "medical practitioner only decision-making, informing consumers", "medical practitioner and consumers as partners in decision-making" and "consumer only decision-making" (Figure 6-7). The analysis of the data also suggests the need to use different medical

practitioner/consumer decision models, depending on the situation. Two examples included: the need for a medical practitioner in surgery to make independent decisions about anaesthetic drugs which may or may not be shared with the consumer post-surgery; and non-critical decisions made by consumers that may or may not be shared with a medical practitioner.

The data also indicated that when one decision-maker is using one decision model and another decision-maker is using a different decision model, miscommunication may arise based on the differences in expectations. The awareness that each decision-maker has partial knowledge of the ADR decision domain, in combination with the emergence of the consumer's role in differential diagnosis suggests the existence of a medical practitioner/consumer decision model which relies on partnership between the decision-makers. The use of this model acknowledges that all decision-makers play an important role, and each have part of the ADR knowledge, which when combined, may result in a decision made with more complete knowledge.

Although the decision models identified within this work arose from the ADR decision domain, it is likely that these models will be found in other areas of medical decision-making. The principles of identifying the decision model the particular consumer and medical practitioner agree to use within a consultation associated with ADR decision-making to decrease confusing and miscommunication can be generalised to other aspects of medical practitioner/consumer decision-making.

7.2.2.5. ADR differential diagnosis

Analysis of the medical practitioner, consumer and expert data, revealed a number of strategies that were used by these decision-makers to make a differential diagnosis. Combining these strategies resulted in an initial understanding of the processes used to make a differential diagnosis between: an ADR; a newly presenting disease or condition; a current disease or condition; and symptoms arising from a nocebo effect.

This emerging model of ADR differential diagnosis (Figure 6-8), is by no means complete. The analysis of these case studies suggested this model as a starting point to understanding these processes. In order to have a more complete understanding, this model would need to be tested

using a larger number of participants, and further work is required to understand how to differentially diagnose an ADR and a nocebo effect.

7.2.2.6. Barriers to the creation of new ADR knowledge

New knowledge about ADRs is created at an international level, a national level and at the level of the individual decision-maker. Although the decision-makers, in particular, the medical practitioners relied on existing ADR knowledge to assist with ADR differential diagnosis the medical practitioners in this study did not report the suspected ADRs for a number of reasons, and therefore did not contribute to the creation of new ADR knowledge.

The other barrier to the development of ADR knowledge is at an individual level. In cases where the prescribing clinician and the medical practitioner were different medical practitioners, in many cases, the prescriber did not receive feedback that s/he had prescribed a drug that may have resulted in an ADR, so the prescribing medical practitioner did not have the opportunity to learn from the incident.

Current literature highlights that ADR reporting is low and discusses the implications for the development of new knowledge. This work adds in a small way to this understanding showing clearly the paradox of the medical practitioner's reliance on current ADR knowledge, the lack of reporting and the apparent lack of awareness of the link between the two.

7.2.2.7. Impact of ADRs on consumers and their future decisions

Triangulation of the case study data highlighted the differences in perspective between the decision-makers relating to the impact and severity of the ADR on the consumer, either directly or indirectly. In several of the case studies, the consumer's reported experience, and the medical practitioner's understanding of the consumer's experience were very different. These case studies demonstrate clearly this miscommunication and the direct impact of this miscommunication had on the medical practitioner/consumer relationship, and on future ADR decisions.

7.2.3. KNOWLEDGE OF THE ADR DECISION DOMAIN THAT CAN BE USED TO PREVENT, DETECT AND MANAGE ADRS

A key theme that has arisen from the analysis of these case studies from a social constructionist perspective is that different decision-makers have different perspectives. Each have partial knowledge, each participate in all decision types although they may play different roles, each has a different understanding of the core ADR concepts and each will have a preferred model of interaction. Awareness of these differences, and the willingness to have a meta-conversation, to clarify expectations and understandings, along side the conversation about the suspected ADR, may assist in communication that works towards combining knowledge, and understanding. The areas of clarification that may need to occur somewhere within the consultation include:

- an agreed medical practitioner/consumer decision model. Awareness that this model is likely to change in different situations, and that different consumers will prefer different models;
- clarification of terms used by each decision-maker;
- awareness that each decision-maker holds important knowledge;
- active sharing of that knowledge at a level that is within the consumer's interest and level of understanding;
- awareness that the medical practitioner's understanding of the consumer's experience may be very different from the consumer's perception of his/her experience. Checking explicitly with the consumer may assist in joint understanding;
- acknowledgment and acceptance of the range of decision types a consumer may use within a medical consultation, as a first step towards working in partnership with the consumer;
- awareness that unless new ADR knowledge is developed, ADR differential diagnosis that relies on this information will become more difficult.

A problem often raised by GPs is that of the lack of time in a short medical consultation, which inhibits additional discussion and clarification. The analysis of these case studies suggests that not taking the time to have these discussions can also be costly.

7.2.4. KNOWLEDGE OF THE ADR DECISION DOMAIN THAT CAN BE USED TO INFORM ADR DECISION SUPPORT

The additional understanding of the ADR decision domain that has emerged from this work may be used when developing ADR decision support systems. It is out of scope of this work to take the outcomes of this work and design an ADR decision support system, however the results point to particular solutions that will be discussed within this section.

7.2.4.1. Consumer's role in ADR decision-making

The role of the consumer in ADR decision-making, and in particular in diagnostic decision-making has clear implications for the development of ADR decision support. That is, that ADR decision support, rather than being a single user system, would benefit from being a multi-user system, and rather than focusing on the medical practitioners as the decision-maker responsible for making ADR diagnostic decisions, acknowledging and incorporating consumer knowledge into the decision-making processes as suggested by the approaches in sections 7.2.4.2 to 7.2.4.4 below.

7.2.4.2. Multiple understandings

Multiple user decision support has been developed to accommodate multiple perspectives. One example is a system called CUP (Collaborative Urban Planner), which has been designed to assist in decision-making from the perspectives of a city council, an architect and someone who has submitted an application for urban development (Monoharan, Taylor & Gardiner, 2002). This system accommodates end user requirements from multiple groups such as the council, architect and applicant. It also assists in collaborative decision-making. Another decision support system that accommodates multiple perspectives is PlanIT, a system designed for land and water resource planning. This system is designed for end-users ranging from farmers to government agencies (Holyland, 2002). These systems, although catering for multiple perspectives and collaborative decision-making have a positivist theoretical perspective, and so assume a single understanding of the underlying concepts.

No multi-user decision support systems based on a social constructionist philosophical perspective have been located, however one group of authors did use a constructionist

philosophical perspective for the development of multiple perspective digital libraries (Tuominen, Talja & Savolainen, 2003). Their approach is to use a combination of nouns and verbs to search the library to accommodate the multiple perspectives found in conversation, rather than using a traditional noun based search facility. This article refers to the use of the constructionist perspective in IT development, but not in the area of decision support.

The results from this work, obtained using a social constructionist epistemology and applied to the area of decision support, suggest a different approach to the traditional multi-user approach. A traditional multi-user database design may include a centralised database or a distributed database that contains information and knowledge obtained from each end-user and is combined into this one database located centrally or in multiple locations. The results from this work suggest a system that would facilitate negotiation between end-users and sharing and exchange of knowledge and the meanings attached to that knowledge, rather than pooling all of the known knowledge into a single database may be more useful within this domain. Multiple users accessing a single database requires the database to be based on a single understanding of the core concepts, and an assumption that the core dataset of knowledge needed to make a 'completely informed decision' is known; two assumptions that did not hold within this ADR decision environment, and from the social constructionist philosophical perspective, possibly do not hold in any multi-user decision domain.

The results of this work point more towards an Agent-based system (agents were discussed in section 2.3.5.5). The assumption behind this suggested approach is that the decision-makers make the decisions, and the agents facilitate the decision-making processes. The end-users may be prompted to negotiate a medical practitioner/consumer decision model that suits the particular decision type and/or decision context. The agents may determine likely or possible knowledge that may be required to assist with the decision, and prompt each decision-maker for the specific knowledge. The knowledge that is relevant may evolve throughout the decision-making process. The agents may prompt decision-makers to clarify meanings.

This type of solution would be enhanced by an electronic medical record, where the agents could search the electronic medical record to find relevant information and bring it to the attention of the decision-makers for their consideration.

7.2.4.3. Using past cases to assist with new decisions

One result from this work was that each decision-maker had partial knowledge, and that each decision-maker used a number of strategies to make a differential diagnosis. Some of the medical specialists used a pattern matching approach; recognition of a pattern of symptoms and drugs in a past case that were similar to the case in question. *The Australian Adverse Drug Reaction Bulletin* is also currently written in the form of cases. This result suggests there may be a role for case-based reasoning within this domain. Past cases that have included knowledge from the consumer, GP, medical specialist and ADRAC, could be collated and stored within a database, to be accessed by any decision-maker when attempting to make a new ADR diagnosis. These cases may be used as a basis of the Agent-based system described in the previous section. Case-based reasoning, however, at this stage, does not accommodate the issue of multiple understandings of core concepts. Further thought and research is required to determine the usefulness of this approach within a social constructionist framework.

7.2.4.4. Combining of partial knowledge

Argumentation (discussed in section 2.3.5.6) is traditionally applied to domains which include argumentative discussion and persuasion dialogue. As discussed previously, it can also be used to assist in facilitating the sharing of knowledge between decision-makers. Given that each decision-maker within the ADR domain holds partial knowledge, and that even with the combination of that partial knowledge, there is likely to be elements of incomplete knowledge, differences of understanding of that knowledge, and differences in opinion of the importance of each piece of knowledge, argumentation may be a useful approach in facilitating discussion and negotiation between decision-makers. Again, it may be useful in particular, when combined with the approaches of agents.

A clear result from this work is the issues that were raised by partial knowledge. In Joanna's case study, there was an example of the advantage of combining that partial knowledge (section 4.4.4.1). In this case study, the medical practitioner had partial information, that is, knowledge of the preparation of Flexitone. Joanna also had partial information, that is, her observations of a reaction to the preparation of Flexitone. When these pieces of information were combined within Dr Carey's interview, new knowledge was generated.

This example indicates that the use of agent technology, specifically agents that use a collaborative model, may be an approach to assist in combining partial knowledge.

7.2.4.5. Implementation of Australian initiatives

Further development of initiatives such as *HealthInsite, Health Online* and *MediConnect* will assist in providing up to date consumer information to Australian consumers. MediConnect will provide summaries of medication records that a medical practitioner can access, with consumer consent, regardless of which medical practitioner, clinic or hospital setting prescribed the drug. ADR decision support would benefit from linking into these current infrastructures and initiatives to ensure interoperability and a co-ordinated approach across Australia.

7.2.4.6. Impact of past decisions on future decisions

A less tangible, but important factor that has arisen from this work, is the impact past experiences of ADRs has had upon the consumer's future decisions surrounding treatment decisions. The implication this factor has for decision support is that as well as incorporating the traditional medical and drug information in ADR decision support systems, including not only the consumer history of past ADRs, but also the impact that history has had on future decisions is important when making new decisions about therapy options. Storing these data in a database is likely not to be useful, as the consumer's perception of what happened during their past experience, and their feelings towards future treatments, are likely to change over time and may change based on the situation. The implication, therefore, is that a decision support system that is based on a technology such as agents may facilitate a discussion aimed at eliciting the consumer's feelings and concerns, especially if there is a history within the consumer medical history of past ADRs, so they can be taken into account when making the current decision.

7.3. Future work

This work has highlighted many possible areas for future work. Each of these will be discussed briefly in this section.

7.3.1. CONSOLIDATION OF THE RESULTS

This work is qualitative and exploratory, which has highlighted a number of areas that may benefit from future work including:

- a study to determine the frequency of use of each of the medical practitioner/consumer decision models that have emerged from this work in a variety of clinical settings;
- a study to determine the percentage of consumers who participate in ADR diagnostic decision-making, including suspecting the ADR;
- the impact of explicitly discussing the preferred medical practitioner/consumer decision model and coming to an agreed model;
- further development of the model of ADR differential diagnosis, and the testing of that emerging theory in clinical settings;
- further clarification of the differences between decision-makers in understanding of the core concepts within the ADR decision domain;
- understanding the role of the pharmacist in the ADR decision domain;
- understanding further the reasons for limited reporting, and developing a strategy that will attempt to take into account the barriers to reporting, whilst increasing the number and quality of ADR reports;
- differential diagnosis between an ADR and a nocebo effect;
- wider use of the methodology and theoretical perspective used in this work to inform the development of decision support followed by evaluation to determine the effectiveness of this methodology in a commercial rather than research context.

7.3.2. POSSIBLE DECISION SUPPORT DIRECTIONS

As mentioned previously, it is beyond the scope of the work of this thesis to develop or design ADR decision support. The analysis of the case studies, however, has suggested: a number general principles that may be applied to the development of ADR decision support; and also some research directions that may be of use within this domain. These have been discussed below. As well as developing the ideas presented in section 7.2.4, some additional ideas have been included below:

- Decision support may inadvertently force decision-makers into a particular decision-making model. Awareness of the different decision models, that different models may be used in different situations, and that different decision-makers will have different preferences for the use of these models is important to consider when developing decision support.

- A number of medical practitioners indicated that they were aware that some drugs are more likely to result in ADRs than others. Determining the reliability of this hierarchy, documenting it and incorporating it into ADR decision support may assist by ordering drugs more or less likely to result in ADRs, assisting in the choice of drug to prescribe, particularly for consumers known to be sensitive to drugs.

- One of the medical practitioners suggested providing consumers with a list of symptoms that they could tick whilst waiting in the waiting room, to elicit knowledge from consumers and facilitate knowledge sharing within a consultation.

- The ADRAC database is only one source of ADR knowledge. The medical practitioners, but in particular medical specialists who specialise in a particular set of drugs have seen a specific group of ADRs regularly, appear to have expert knowledge of particular types of ADRs. Accessing this knowledge and making it available to non-expert ADR decision-makers may be another way of gathering new ADR knowledge and disseminating it to other ADR decision-makers.

- Develop an ADR Case Based Reasoning system to assist in real-time ADR decision-making and as an educational training tool. As discussed in section 2.3.5.4, using the ADR domain, new cases, hypothesised by the ADR decision-makers could be tested by submitting the new cases to ADRAC. ADRAC could then verify or otherwise the 'correctness' of the new case, and determine if it were to be added to the database. If anyone were to update the database, there would be a risk that the integrity of the cases would be compromised.

APPENDIX A

Case Studies

The case study data is in Volume two of this thesis. The reasoning behind this has been explained in section 3.6, ethical considerations.

APPENDIX B

Consumer plain language statement

Project Explanation for Participants – Consumers
(Plain language statement)
Attachment 1A

Project Title: Understanding unwanted reactions to medications.

Principal Investigator: Michelle O'Brien
Senior Investigator: Dr. John Yearwood

Project Description

The aim of this project is to understand more about the unwanted reactions people may have to medications in rare but serious situations. It is hoped that an in-depth understanding of these reactions will assist in the ability to prevent, detect, and if necessary manage these reactions in the future.

This study begins with a Consumer (patient) focus. (From this point on, the Consumer or Patient will be referred to as the participant). The participant who has experienced the reaction is the only person who was present throughout the entire course of the reaction. A Doctor may only see a snap shot of the reaction. There may be more than one Doctor involved over the time the participant experienced the reaction. Information about the reaction may be in more than one medical file. Part of it may be in the family GP's file and some in an after hours-emergency clinic's file. The information about this reaction, therefore is spread between the participant, the Doctors involved and multiple medical files.

Each person or group of people have different understandings of what is happening. A participant is present throughout the entire reaction, but generally has no medical training. A Doctor is present when the participant is in his/her clinic only, but can interpret what is seen using an understanding of medicine. If the reaction is serious enough, it may be sent to a group of experts in Canberra for their opinion. They have expertise in reactions to medications, but only have access to the limited information sent to them by the Doctor, and have no access to the participant. Each person or group of people only have part of the total information about the reaction.

In this study, we would like to gather all of the information about the reaction in order to understand it more fully. We plan to interview participants who have experienced reactions to understand them from their point of view. The next stage is to find all of the pieces of the medical history that relate to each reaction that are stored in medical files. The third stage is to show this information (without identifying the participant) to a group of experts to gather their opinion of the reaction. The final stage is to discuss each case with a group of General Practitioners.

Specifically, having gathered all of this information, we are interested in identifying the critical things that happened throughout the reaction, and the decisions made by the participants and Doctors, leading up to, during and following a serious reaction to a medication.

The ultimate aim of this project is to use the information to develop technology that can be used to assist in the prevention, efficient detection, and management of reactions caused by medications.

Participant Screening

There are some conditions that a participant may have that may make the study of an unwanted reaction to medication very complex. If a participant has any of these conditions, they will not be able to participate in the study. The first stage, therefore, will be to ask the participant, verbally, if they meet the criteria outlined in the advertisement:

To participate in the study, a participant will need to:

- suspect they have experienced a moderate to severe reaction to medication within the last 6-12 months;
- be over 18 at the time of the reaction;
- not be taking recreational drugs either at the time of the study or at the time of the reaction;
- not have any conditions that may affect his or her ability to report the experience. This may include language disorders, cognitive (processing or memory) disorders, or some psychiatric conditions.

Participant Involvement

Each participant, who meets the criteria, will be asked to do five things:

- Participate in an interview with the Principal Investigator (Michelle O'Brien), which will be approximately an hour in length. The aim of the interview will be for the participant to talk about his/her experience of having a reaction to a medication. The interview will be tape recorded, and then transcribed.

- Using a time line, write down the details of what happened throughout the reaction. This will include symptoms, medical clinics, medications, and doses. Obviously it may be difficult to remember all of the information, but this process will assist in recalling as many facts about the event as possible.

- Think about the events that preceded and followed the reaction, and indicate anything the participant would do differently if they were to have known the reaction was going to occur, and anything they would have liked their medical practitioner to have done differently. The aim of this component is to use the advantage of hindsight to find strategies to assist in the prevention, early detection or management of reactions in the future.

The participant will be asked to sign a consent form to allow:

- the principal researcher to collect the information from the participant's medical files on the dates indicated by the participant, from the clinics indicated by the participant .
- the principal researcher to pass on the information gathered about the reaction (without identifying the participant), to the Therapeutics Goods Administration – Adverse Drug Reactions Department who are experts in identifying medications with reactions, in order to obtain an expert opinion on the reaction.
- the principal researcher to show the information gathered about the reaction to a group of general practitioners, in order to understand which pieces of information are the most important to a Doctor when attempting to prevent, diagnose or manage medication reactions. Again the information would not include any information that identifies the participant. In the case where a Doctor did recognise the history, they would be required to keep this information to themselves in the same way that they do not discuss information about their patients now.

The participant will also be asked to nominate their family GP so that if there is any information that the participant needs to know, it can be passed onto their family GP.

We understand that this information is highly confidential and will be treated accordingly. The only information collected will be the information that the participant has given consent to be collected, and it will only be used for the purposes outlined in this document. The only person to have access to the participant's identify will be the principal researcher. The information will be de-identified. That means that there will be no names and addresses stored with the information, just a code.

At the end of the project, participants will be free to access the results of the research by contacting the principal researcher. If, during the course of the project, information about the a reaction is discovered, that is important for the individual to know, the information will be sent to the family GP, and the participant will be notified so he/she can make an appointment to discuss this with the Doctor if required.

Time commitment

Each participant will be asked to attend a 1-hour session with the principal researcher in a location that is suitable. Participants may need to be contacted and asked to attend another meeting if further information is required after looking in detail at the information. One example may be if there appears to be some details missing.

Benefits of the study

This study will provide society with more information about what actually occurs when a participant experiences a serious reaction to a medication. It is hoped that the information

gained from the study will assist people developing information technology tools that will be more closely aligned with the needs of the Doctors and participants, specifically to prevent, detect early and manage more effectively reactions to medications. It will also be used to provide medical practitioners with a different view of an adverse medication reaction from the view they usually see, which may provide them with additional insight that will assist in their practice.

Withdrawal from the study

Any participant is free to withdraw and/or to withdraw their permission for their interview or medical information to be used in the study at any point in time.

Any questions regarding the project titled "Understanding unwanted reactions to medications" can be directed to the Principal Researcher, Michelle O'Brien, of the School of Information Technology and Mathematical Sciences on telephone number 041 856 8010.

De-briefing support

If, during or following the study, you felt the need to speak with a counsellor, services are available through one of the following sources.

Clinical Health
[clinic details]
(To access this service you will need a referral from a General Practitioner)

Or in the event of immediate support

[Private psychologist's name]
Private Psychologist
[Telephone details].

[Private psychologist's name]
Private Psychologist
[Telephone details].

* University of Ballarat will fund debriefing if this is required. This will include an individual de-briefing session, and up to four counselling sessions. If you require this service, you are free to access it without notifying the University.

Thank you for your interest in the study.

Michelle O'Brien
Principal Researcher
School of Information Technology and Mathematical Sciences
University of Ballarat

m.obrien@ballarat.edu.au

Should you (ie. the participant) have any concerns about the conduct of this research project, please contact the Executive Officer, Human Research Ethics Committee, Office of Research, University of Ballarat, PO Box 663, Mt Helen VIC 3353.
Telephone: (03) 5327 9765.

APPENDIX C

Consumer consent form

Consumer Code:……..(For office use only)

I, ……..…

of……

agree to the principal investigator, Michelle O'Brien:

- speaking with each of the clinicians who treated me during the following episodes of care, interviewing them, and collating the medical view of the suspected reaction.

Clinic Episode of Care (Date)
……..……
……..……

- compiling the information I have provided on the time-line attached, the information provided by the medical personnel I consulted, and showing this information that will not contain any information that will expose my identity, to the Therapeutic Goods Administration – Adverse Drug Reactions Department, for an expert opinion on my case;

- compiling the information I have provided on the time-line attached, information provided by the medical personnel I consulted, and showing this information that will not contain any information that will expose my identity, or the identity of the clinics or Doctors involved in my case, to a group of General Practitioners from the Ballarat Division of General Practitioners. I understand that it is possible that one of these Doctors will recognise my details, but also understand that if they do, they will maintain my confidentiality in the same way they are required to do when I visit their clinic;

The research program in which I am being asked to participate has been explained fully to me, verbally and in writing, and any matters on which I have sought information have been answered to my satisfaction.

I understand that:

- all information I provide (including questionnaires) will be treated with the strictest confidence and data will be stored separately from any listing that includes my name and address
- aggregated results will be used for research purposes and may be reported in scientific and academic journals

- I am free to withdraw my consent at any time during the study in which event my participation in the research study will immediately cease and any information obtained from it will not be used.

SIGNATURE: . . . . . **DATE**: . . . . . .

APPENDIX D

Introductory letter to medical practitioners

[Date]

Dear Dr [medical practitioner],

Re: - the PhD study "Understanding unwanted reactions to medications".

[Consumer's name], a consumer of your practice, has agreed to be a participant in the above study. She has participated in the first phase as outlined in the enclosed document outlining the project in detail - Attachment 1B.

The project was approved by the following ethics committees:
- [University Ethics committee] – 13th June, 2002
- [Combined Hospitals Ethics Committee (hospitals involved in the study)] – 8th August, 2002.

I am wondering if you would be prepared to participate in the second phase of the study please? Your participation would involve the following: -

- Reviewing [Consumer's name] case notes in relation to a suspected reaction to pain management medication,
- An interview with me to discuss the suspected reaction from a medical perspective. (Remuneration is available at the rate of $100/hr).

Obviously confidentiality and privacy are key issues within this project. Please find enclosed: -

- A copy of the consent form signed by [Consumer's name],
- A consent form for you to sign if you would be prepared to participate,
- An information package for your information about the project.

If you would like to discuss this further or to make a time, please contact me by e-mail on m.obrien@ballarat.edu.au or 041 856 8010. I understand you are extremely busy, so if I don't hear from you within a week, I will ring you to discuss this further.

Thanks very much for you assistance,

Michelle O'Brien
Principal Researcher
School of Information Technology and Mathematical Sciences
University of Ballarat
m.obrien@ballarat.edu.au

APPENDIX E

Medical plain language statement

Project Explanation for Participants – Medical Practitioners
(GPs who provide access to medical records, GPs in GP forums, and TGA personnel)

Attachment 1B

Project Title: Understanding unwanted reactions to medications.

Principal Investigator: Michelle O'Brien
Senior Investigator: Dr John Yearwood

Project Description

The aim of this project is to learn more about adverse drug reactions (ADRs). At this stage, some information is known about some ADRs. For example:

- Type A reactions are related to the pharmacology of a drug.
- Type B reactions are less predictable, generally more serious and may be related to the individual Consumer (eg hypersensitivity)
- Drug/Drug interactions occur when one drug interacts with another drug which results in an unwanted reaction.
- Contra-indications exist for some drugs that are known to cause problems with particular conditions. Contra-indications may possibly warn against taking a particular drug, and in some circumstances, certain drugs must never be taken.

Most ADR information contains large amounts of uncertainty. ADRs that have been documented may occur for some people with some condition in some circumstances.

It is also known that GPs and Hospital Doctors find it difficult to access the ADR information for the specific Consumer at the right time.

This study will investigate the GP/Consumer decision environment to find the critical decision points and contexts in the prescribing process to inform decision support.

This study begins with a Consumer (patient) focus. The person who has experienced the reaction is the only person who was present throughout the entire course of the reaction. A Doctor may only see a snap shot of the reaction. There may be more than one Doctor involved

over the time the Consumer is experiencing the reaction. Information about the reaction may be in more than one medical file. Part of it may be in the family GP's file and some in an after hours-emergency clinic's file. The information about this reaction therefore is spread between the Consumer, the Doctors involved and multiple medical files.

Each person or group of people have different perspectives. A Consumer is present throughout the entire reaction, but generally has no medical training. A Doctor is present when the Consumer is in his/her clinic only, but can interpret what is seen using an understanding of medicine. If the reaction is serious enough, it may be sent to ADRAC (Adverse Drug Reactions Advisory Committee) in Canberra. ADRAC have expertise in reactions to medications, but only have access to the limited information sent to them by the Doctor, and have no access to the Consumer. Each person or group of people only have part of the total information about the reaction.

In this study, we plan to gather all of the information about reactions in order to understand them more fully. We plan to interview Consumers who have experienced reactions to understand the reaction from their point of view. The next stage is to find all of the pieces of the medical history that relate to the reaction that are stored in medical files. The third stage is to show this information (de-identified) to the Therapeutics Goods Administration – Adverse Drug Reactions Department, for their opinion of the reaction. The final stage is to discuss each case (again, de-identified) in a GP Forum.

Specifically, having gathered all of this information, we are interested in identifying the critical events that happened throughout the reaction, and the decisions made by the Consumers and Doctors, leading up to, during and following a serious reaction to a medication.

The ultimate aim of this project is to use the information to develop decision support technology that can be used to assist in the prevention, efficient detection, and management of reactions caused by medications.

Consumer Screening

There are some conditions that a Consumer may have that may make the study of an unwanted reaction to medication very complex. If a Consumer has any of these conditions, they will not be able to participate in the study. Before being accepted into the study, the Consumer will be asked verbally if they meet the criteria in the advertisement:

To participate in the study, a participant will need to:

- suspect they have experienced a moderate to severe reaction to medication within the last 6-12 months;
- be over 18 at the time of the reaction;
- not be taking recreational drugs either at the time of the study or at the time of the reaction;
- not have any conditions that may affect his or her ability to report the experience. This may include language disorders, cognitive (processing or memory) disorders, or some psychiatric conditions.

Group 1. Consumer Involvement

Each Consumer who meets the criteria will be asked to do five things:

- Participate in an interview with the Principal Investigator (Michelle O'Brien), which will be approximately an hour in length. The aim of the interview will be for the person to talk about their experience of having a suspected reaction to a medication. The interview will be tape recorded, and then transcribed.

- Using a time line, the Consumer will be asked to write down the details of what happened throughout the suspected reaction. This will include symptoms, medical clinics, medications, and doses. Obviously it may be difficult to remember all of the information, but this process will assist in recalling as many facts about the event as possible.

- The Consumer will be asked to think about the events that preceded and followed the reaction, and indicate anything they would do differently if they were to have known the reaction was going to occur, and anything they would have liked their medical practitioner to have done differently. The aim of this component is to use the advantage of hindsight to find strategies to assist in the prevention, early detection or management of reactions in the future.

The Consumer will be asked to sign a consent form to allow:

- the principal researcher to collect the information from their medical files on the dates indicated by the person, from the clinics indicated by the person .
- the principal researcher to pass on the information gathered about the reaction (without identifying the person), to a group of experts at the Therapeutics Goods Administration – Adverse Drug Reactions Department who are experts in identifying medications with reactions, in order to obtain an expert opinion on the reaction.
- the principal researcher to show each case gathered about the reaction to a group of general practitioners, in order to understand which pieces of information are the most important to a Doctor when attempting to prevent, diagnose or manage medication reactions. Again the information would not include any information that identifies the person. In the case where a Doctor did recognise the history, they would be required to keep this information to themselves in the same way that they do not discuss information about their patients now.

The Consumer will also be asked to nominate their family GP so that if there is any information that the person needs to know, it can be passed onto their family GP.

At the end of the project, Consumers will be free to access the results of the research by contacting the principal researcher. If, during the course of the project, information about the a reaction is discovered that is important for the individual to know, the information will be sent to the family GP, and the person will be notified so he/she can make an appointment to discuss this with the Doctor if required.

Group 2. Interview with Medical Personnel.

Doctors who have treated the Consumers with suspect ADRs will be sent an information package including background information about the study, a consent form if they wish to

participate in the study and a letter requesting information from relevant medical records or components of the medical records that pertain to the specific suspected ADR as identified by the Consumer. The GP will be asked to extract key information using the Consumer medical record data collection form, or to allow the principal researcher to extract these data under his/her supervision. Data will be de-identified before it leaves the GP's office. The GP will be able to allocate codes to the data prior to releasing it.

Group 3. TGA ADR involvement

Staff at the TGA will be sent background information about the project, asked to review each case using their expertise in ADRs, and then to fill in a questionnaire for each case. This information will be used as an "expert" view of the case. It will also be used to determine the key decisions, events and pieces of data that influence the prevention, detection or management of an ADR, from the perspective of the expert.

Group 4. GP Forums

GPs interested in attending the GP forums will be sent background information about project and asked to fill in a participation consent form. Each GP will be asked to attend a series of four forums of one hour each to be held at the [GP division]. The content of these forums will include background information about ADRs, and then each case (de-identified) will be presented for the GP group to comment on. Again, the aim will be for the GPs to view the Consumer time lines and medical record information in order to identify key decisions, events and pieces of data that influence the prevention, detection and management of an ADR from the perspective of a GP.

Privacy

Medical records cannot be accessed for this project without written informed Consumer consent. Each Consumer has been provided with background information that has been written in plain language text. They have also been asked to sign an informed consent form to allow their data (collected in an interview, and data from their medical records) to be used in the study.

The data collected for the study will only be used for the purposes disclosed the document/s provided to participants and so is within the privacy guidelines.

Confidentiality

Confidentiality will be maintained within this project.

The Consumer participants will be identified to the medical clinics that hold their medical files in order to provide the consent required, and in order to access these files. Once a case has been collated, this includes the Consumer view of the suspected reaction and the medical file information, the data will then be de-identified, so that the Consumer, medical clinics or individual Doctors will not be able to be identified. The names and addresses that pertain to the codes will be stored separately from the data which will only be identified by codes.

Each Consumer will be provided with a code eg. C10. Each clinic for each Consumer will be issued a code eg. GP1. The code for the first GP clinic this Consumer visited, therefore would be C10GP1.

The only time the codes, Consumer and medical file data will be joined together again, are if the TGA ADR department were to identify information about the Consumer's condition that was critical for the future health of the Consumer that the GP should know about. In this case, the data would be identified and provided to the TGA ADR department. They would then maintain the confidentiality of these data in the same way they maintain the confidentiality of ADR reports that are sent to them on a regular basis.

Data Storage

During the study

All original data (including tapes and medical file data) will be stored in a locked filing cabinet in the principal researcher's office. Once the data have been de-identified and transcribed, the original data will be stored in the data storage office (a locked office) in the school of ITMS. The documents linking the codes to the participants will be stored in a locked filing cabinet in the supervising researcher's office – Dr John Yearwood.

Following the completion of the study (all data needs to be stored for five years following the completion of the study)

All original data (including tapes and medical file data) that have identifying data will be destroyed. All transcripts that have been de-identified will be stored in a locked filing cabinet in a locked data storage room in the school of ITMS. All data that have participant details and the associated codes will be stored in a locked filing cabinet in the principal researcher – Dr John Yearwood's office.

De-briefing available

In the event that discussing an ADR results in either a Consumer or GP requiring de-briefing, the following supports will be available.

Consumer Support

Clinical Health
[clinic details]
(To access this service you will need a referral from a General Practitioner)

Or in the event of immediate support

[Private psychologist's name]
Private Psychologist
[Telephone details].

[Private psychologist's name]
Private Psychologist
[Telephone details].

(Although it is not anticipated that participation will cause participants distress, in the event that a participant is distressed by participating in the study, the university will fund up to four counselling sessions. Participants are free to contact these services without revealing this to the University. If a participant were to require further support, the psychologist the Consumer is seeing, will arrange a follow up service).

General Practitioner's support

Ballarat and District Division of General Practitioners de-briefing service will be available for any GPs requiring support.

Time commitment

Consumers.

Each Consumer will be asked to attend a 1-hour session with the principal researcher in a location that is suitable. Participants may need to be contacted and asked to attend another meeting if further information is required after looking in detail at the information. One example may be if there appears to be some details missing.

GPs providing access to medical records.
The time commitment may be up to half an hour per clinic per medical record accessed.

GP Forums

The time commitment will be 4x1 hour sessions plus travel time to the BDDGPs, over a period of four weeks.

TGA ADR experts

The time commitment will be up to one hour per case for up to 30 cases. A possible total commitment of 30 hours over a period of six months.

Benefits of the study

This study will provide society with more information about what actually occurs when a person experiences a serious reaction to a medication. It is hoped that the information gained from the study will assist people developing information technology tools that will be more closely aligned with the needs of the Doctors and Consumers, specifically to prevent, detect early and manage more effectively reactions to medications. It will also be used to provide medical practitioners with a different view of an adverse medication reaction from the view they usually see, which may provide them with additional insight that will assist in their practice.

Withdrawal from the study

Any person is free to withdraw and/or to withdraw their permission for their interview or medical information to be used in the study at any point in time.

Any questions regarding the project titled "Understanding unwanted reactions to medications" can be directed to the Principal Researcher, Michelle O'Brien, at the School of Information Technology on telephone number 041 856 8010.

Thank you for your interest in the study.

Michelle O'Brien
Principal Researcher
School of Information Technology and Mathematical Sciences
University of Ballarat
m.obrien@ballarat.edu.au

Should you have any concerns about the conduct of this research project, please contact the Executive Officer, Human Research Ethics Committee, Office of Research, University of Ballarat, PO Box 663, Mt Helen VIC 3353. Telephone: (03) 5327 9765.

APPENDIX F

Medical consent form

UNIVERSITY OF BALLARAT

INFORMED CONSENT
For Medical Staff who treated the Consumers in the study,
GP Forums and TGA ADR Experts.

Code number allocated to the participant (office use only)……. . . . . .

Consent (fill out below)

. . . . . of . . . . . .
. . . . . .

hereby consent to participate in the above research study.

The research program in which I am being asked to participate has been explained fully to me, verbally and in writing, and any matters on which I have sought information have been answered to my satisfaction.

I understand that:

- all information I provide (including questionnaires) will be treated with the strictest confidence and data will be stored separately from any listing that includes my name and address
- aggregated results will be used for research purposes and may be reported in scientific and academic journals
- I am free to withdraw my consent at any time during the study in which event my participation in the research study will immediately cease and any information obtained from it will not be used.

SIGNATURE: . . . . . **DATE**: . . . . . .
. . .

APPENDIX G

Expert questionnaire

TGA ADR expert Questionnaire

Participant code ……..……..

Please refer to background document for information about the project.

Each of the cases include information the Consumer has provided about what they suspect may be an ADR, and the medical records for the dates the Consumer feels they experienced the ADR.

For each case, can you please answer the following questions?

Can you please determine a possible diagnosis/es for the symptoms described in the case?

How certain are you of this diagnosis?

If you consider the diagnosis to be an ADR, using the advantage of hindsight and the cumulated medical histories

a. Are there any things that could have been done to prevent the reaction?

b. What, if anything, could have been done to detect the reaction earlier?

c. What, if anything, could have been done to manage the ADR more effectively?

What, in your opinion, are the key pieces of information, from within the case, that were used to make the diagnosis?

What were the critical decisions do you feel were made throughout this process?

a. By the doctor/s

b. By the Consumer

c. Collaborative decisions.

What were the critical events you feel were made throughout this process?

Are there any other factors in this case that you feel are significant? If so, what are they and why do you feel they are significant?

APPENDIX H

List of questions for consumer interviews

Initial questions

- Tell me what happened, leading up to, during and following your suspected reaction?
- (Prompted for events leading up to, during and following the suspected reaction, including medications, dosages, clinics, doctors if required).
- Who diagnosed the suspected reaction, and how certain is the diagnosis?
- Was there anything that hindered or obstructed the diagnosis or management of the suspected ADR?
- What communication was there between yourself and your doctors, and between the doctor/s and the hospital? (In cases when there was more than one doctor involved)
- Have you had a reaction to a medication in the past?
- How long have you been seeing your current doctor? Do you regularly see the same doctor, or do you move between GPs?
- Using hindsight, is there anything you do differently if you were faced with this situation again to either prevent or detect the suspected reaction?
- Again, using hindsight, is there anything would you have liked your doctor/s to do differently?
- What additional medications were you taking at the time of the suspected reaction, including prescription, over the counter, and complementary (herbal) preparations?

Additional information gathered in later interviews

- Asking about the history of pre-existing conditions to provide context for the experience of the suspected ADR,
- exploring the risk of the medication versus the benefits of the medication weighed up against the risks of not treating the condition,
- consumer doctor decision-making models,
- feelings and impact of the suspected ADR,
- sources of information used by the consumer to assist with decision-making,
- consumer decision types surrounding ADRs,
- other people in the consumer decision-making environment that were involved in the decision-making processes and,
- understanding of the terminology of "side effect" versus "drug reaction"

APPENDIX I

Time line of events

Consumer ID:-

Date of Interview:-

Date								
Event								
Description								
Treatment								
Medication/s								
Dose								

APPENDIX J

Inventory of data stored in an NVivo database

Document type	Document Name
Memo	C02 - Memo
Consumer Interview	C02 - Toni
Consumer Interview	C04 - Julie
	C04 - Memo
	C04 - Memo 2
	C04 - Memo 3
	C04 - Memo 4
Consumer Interview	C05 - Kay
Consumer Interview	C06 - Helen
	C06 - Memo
	C06 - Memo 2
Consumer Interview	C07 - Mary
Consumer Interview	C08 - Belinda
	C08 - Memo
	C08 - Memo 2
	C09 - Memo
Consumer Interview	C09 - Tim
Consumer Interview	C10 - Edward
Consumer Interview	C11 - Irene
Consumer Interview	C12 - James
Consumer Interview	C13 - Joanna
	C13 - Memo
Consumer Interview	C14 - Bob
	C14 - Memo
	C14 - Memo 2
Consumer Interview	C15 - Kerry
Consumer Interview	C16a - Robyn
Consumer Interview - husband	C16b - Thomas
	C17 - Memo 2
Consumer Interview	C17 - Paul
Medical practitioner Interview	Interview with C02GP1 - Dr Barns
	Interview with C02GP1 - Memo
Medical practitioner Interview	Interview with C05H1 - Dr Green
Medical practitioner Interview	Interview with C05SP1- Dr Nash
Medical practitioner Interview	Interview with C06H1 - Dr Stevens
Medical practitioner Interview	Interview with C07SP1 - Dr O'Neil
Medical practitioner Interview	Interview with C09GP1- Dr Price

Medical practitioner Interview	Interview with C11SP1 - Dr James
Medical practitioner Interview	Interview with C13GP1 - Dr Carey
	Interview with C13GP1 - Memo
Medical practitioner Interview	Interview with C17GP1 - Dr Lang
	Interview with C17GP1 - Memo
Expert Questionnaire	TGA 3 Questionnaire C07
Expert Questionnaire	TGA 3 Questionnaire C16
Expert Questionnaire	TGA 2 Questionnaire C02
Expert Questionnaire	TGA 2 Questionnaire C04
Expert Questionnaire	TGA 2 Questionnaire C05
Expert Questionnaire	TGA 2 Questionnaire C06
Expert Questionnaire	TGA 2 Questionnaire C08
Expert Questionnaire	TGA 2 Questionnaire C09
Expert Questionnaire	TGA 2 Questionnaire C10
Expert Questionnaire	TGA 2 Questionnaire C11
Expert Questionnaire	TGA 2 Questionnaire C12
Expert Questionnaire	TGA 2 Questionnaire C13
Expert Questionnaire	TGA 2 Questionnaire C14
Expert Questionnaire	TGA 2 Questionnaire C15
Expert Questionnaire	TGA 2 Questionnaire C17
Expert Questionnaire	TGA1QuestionsC07
Expert Questionnaire	TGA1QuestionsC10
Expert Questionnaire	TGA1QuestionsC11
Expert Questionnaire	TGA1QuestionsC12
Expert Questionnaire	TGA1QuestionsC13
Expert Questionnaire	TGA1QuestionsC14
Expert Questionnaire	TGA1QuestionsC15
	TGA1QuestionsC15 - Memo
	TGA1QuestionsC15 - Memo 2
Expert Questionnaire	TGA1QuestionsC16
Expert Questionnaire	TGA1QuestionsC17
Expert Questionnaire	TGA1QuestionsCO2
	TGA1QuestionsCO2 - Memo
	TGA1QuestionsCO2 - Memo 2
Expert Questionnaire	TGA1QuestionsCO4
Expert Questionnaire	TGA1QuestionsCO5
	TGA1QuestionsCO5 - Memo
	TGA1QuestionsCO5 - Memo 2
	TGA1QuestionsCO5 - Memo 3
	TGA1QuestionsCO5 - Memo 4
Expert Questionnaire	TGA1QuestionsCO6
Expert Questionnaire	TGA1QuestionsCO8
	TGA1QuestionsCO8 - Memo
Expert Questionnaire	TGA1QuestionsCO9

APPENDIX K

Questions for medical practitioner interviews

- Could you please review case notes and fill in time-line of events from medical perspective? (This was changed to ask if they could review the medical notes and then explain what they believed happened).
- Do you feel this medication caused these symptoms? If so, to what degree of certainty?
- How easy or difficult was it to determine if this was an ADR, a pre-existing disease, or a new disease?
- How did you come to your diagnosis?
- What were the key factors?
- What model do you feel was used in the diagnosis and treatment options?
- Was it a joint decision with (consumer name)?,
    - initially observed and diagnosed by the consumer,
    - initially observed and diagnosed by you?
- How did the consumer assist or otherwise the detection and/or management of the ADR?
- What sources of information did you use?
    - External
    - From Medical knowledge
    - From knowledge of consumer
    - From Consumer
- Were the resources used effective?
- Were there any resources that are available that you would have liked to have been able to use, but were unavailable?
- Were there any resources that are currently not available that you would like to see become available (some that don't yet exist)?
- Is there any history of reactions to medications in the file?
- Do you see any difference between side effects and ADRs? If so, what are the differences?
- Is there anything you would do differently if faced with this same situation again using the advantage of hindsight?
- Is there anything you feel you would like the consumer to have done differently if faced with this same situation again?
- In the data so far, it appears that for some people, symptoms they know could be caused by a drug (side effects) were tolerated, but unexpected symptoms resulted in increased anxiety – what are your thoughts about this?

- Did you report this suspected reaction to TGA?
    - Why?
    - Why not?
- What do you believe was the impact of this suspected ADR was on the Consumer?
- How would you describe the severity of this suspected reaction?

References

ADRAC. (2001). *Reporting Adverse Reactions*. Retrieved, 2003, from the World Wide Web: www.health.gov.au/pubhlth/strateg/immunis/adrac.htm

American Society of Consultant Pharmacists. (1998). *Guidelines on Detecting and Reporting Adverse Drug Reactions in Long-Term Care Environments*. Retrieved March, 2005, from the World Wide Web: http://www.ascp.com/public/pr/guidelines/adverse.shtml

American Society of Health-System Pharmacists. (1995). *ASHP Guidelines on Adverse Drug Reaction Monitoring and Reporting*. Retrieved March, 2005, from the World Wide Web: http://www.ashp.org/bestpractices/MedMis/MedMis_Gdl_ADR.pdf

Bankhead, C. (1999). Educated Patients Make Better Stone Tx Decisions. *Urology Times, 27*(11), 30.

Bannwarth, B., Queneau, P., Carpentier, F., Guliana, J.-M., Bouget, J. & Trombert, B. (2003). Hospital Visits Caused by Adverse Drug Reactions: Incidence and Preventability Assessed in French Primary Care/Emergency Departments. *Drug Safety, 26*(2), 133-134.

Barber, K. S., Han, D. C. & Liu, T. H. (2000). *Coordinating Distributed Decision Making Using Reusable Interaction Specifications*. Paper presented at the Proceedings of the Third Pacific Rim International Workshop on Multi-Agents.

Barnett, G. O., Famiglietti, K. T., Kim, R. J., Hoffer, E. P. & Feldman, M. J. (1998). *Dxplain on the Internet*. Paper presented at the Proceedings of the 1998 AMIA Annual Fall Symposium.

Barsky, A. J., Saintfort, R., Rogers, M. P. & Borus, J. F. (2002). Nonspecific Medication Side Effects and the Nocebo Phenomenon. *Journal of American Medicine Association, 287*(5), 622 - 627.

Bates, D. (2000). Using Information Technology to Reduce Rates of Medication Errors in Hospitals. *British Medical Journal, 320*(March), 788-791.

Bates, D. W. (1999). Frequency, Consequences and Prevention of Adverse Drug Events. *Quality Clinical Practice, 19*, 13-17.

Beliakov, G. & Warren, J. (2001). Fuzzy Logic for Decision Support in Chronic Care. *Artificial Intelligence in Medicine, 21*, 209-213.

Benson, J. & Britten, N. (2002). Patients' Decisions About Whether or Not to Take Antihypertensive Drugs: Qualitative Study. *British Medical Journal, 325*(7369).

Better Health Channel (2003). State Government of Victoria, Australia. Retrieved 4th April, 2004, from the World Wide Web: www.betterhealth.vic.gov.au

Blaikie, N. (2000). *Designing Social Research.* Cambridge, UK: Polity Press in association with Blackwell Publishers Ltd.

Bortnichak, E. A. & Dai, W. S. (1999). Epidemiologists and Adverse Event Data - a Challenge to the Field. *Pharmacoepidemiology and Drug Safety, 8*, 457-461.

Britten, N., Stevenson, F. A., Barry, C. A., Barber, N. & Bradley, C. P. (2000). Misunderstandings in Prescribing Decisions in General Practice: Qualitative Study. *British Journal of Medicine, 320*(7233), 484-488.

Broadstock, M. & Michie, S. (2000). Processes of Patient Decision Making: Theoretical and Methodological Issues. *Psychology and Health, 15*, 191-204.

Brown, J. D. & Landry, F. J. (2001). Recognizing, Reporting, and Reducing Adverse Drug Reactions. *Southern Medical Journal, 94*(4), 370-373.

Bruera, E., Willey, J. S., Palmer, J. L. & Rosales, M. (2001). *Treatment Decisions for Breast Carcinoma. Patient Preferences and Physician Perceptions.* Paper presented at the American Society of Clinical Oncology 37th Annual Meeting, San Francisco, California.

Caldwell, R. (2000). Alerting Staff to Medication Errors. *Health Management Technology, 21*(Aug), 52.

Carbogim, D. V., Robertson, D. & Lee, J. (2000). Argument-Based Applications to Knowledge Engineering. *The knowledge engineering review, 15*(2), 119-149.

Carroll, J. S. & Johnson, E. J. (1990). *Decision Research: A Field Guide*: Sage Publications, Inc.

Caspi, O. (2002). Letter to the Editor. *Journal of American Medicine Association, 287*(19), 2502.

Cendrowska, J. & Bramer, M. A. (1984). A Rational Reconstruction of the Mycin Consultation System. *International Journal of Man-Machine Studies, 20*(3), 229-317.

Charavell, M., Bremond, A., Moumjid-Ferdjaoui, N., Mignotte, H. & Odile Carrere, M. (2001). Shared Decision-Making in Question. *Psycho-oncology, 10*, 93-102.

Checkland, P. B. (1981). *Systems Thinking, Systems Practice*. Chichester, UK: Wiley.

Cohen, J. S. (2000). Avoiding Adverse Reactions. *Geriatrics, 55*(2), 54-60.

Coulter, A., Entwistle, V. & Gilbert, D. (1999). Sharing Decisions with Patients: Is the Information Good Enough? *British Medical Journal, 318*, 318-322.

Coulter, D. M. (2000). The New Zealand Intensive Medicines Monitoring Programme in Pro-Active Safety Surveillance. *Pharmacoepidemiology and Drug Safety, 9*, 273-280.

CRM. (2000). *Consumer Reports on Medicines - CRM - Policy and Practice.* Paper presented at the First International Conference on CRM, Sigtuna, Sweden.

Crook, J. A. (2001). How Do Expert Mental Health Nurses Make on-the-Spot Clinical Decisions? A Review of the Literature. *Journal of Psychiatric and Mental Health Nursing, 8*(1), 1-5.

Crotty, M. (1998). *The Foundations of Social Research: Meaning and Perspective in the Research Process.* St Leonards, Australia: Allen and Unwin.

Dean, B., Schachter, M., Vincent, C. & Barber, N. (2002). Causes of Prescribing Errors in Hospital Inpatients: A Prospective Study. *The Lancet, 359*(April 20), 1373-1378.

Dormann, H., Criegee-Rieck, M., Neubert, A., Egger, T., Geise, A., Krebs, S., Schneider, T., Levy, M., Hahn, E. & Brune, K. (2003). Lack of Awareness of Community-Acquired Adverse Drug Reactions Upon Hospital Admission: Dimensions and Consequences of a Dilemma. *Drug Safety, 26*(5), 353-363.

Eddy, D. (2005). Evidence-Based Medicine: A Unified Approach. *Health Affairs, 24*(1), 9-17.

Edwards, I. R. & Aronson, J. K. (2000). Adverse Drug Reactions: Definitions, Diagnosis, and Management. *Lancet, 356*, 1255-1259.

Elstein, A. S. & Schwarz, A. (2002). Evidence Base of Clinical Diagnosis: Clinical Problem Solving and Diagnostic Decision Making: Selective Review of the Cognitive Literature. *British Journal of Medicine, 324*, 729-732.

Emanuel, E. J. & Emanuel, L. L. (1992). Four Models of the Physician-Patient Relationship. *JAMA: Journal of American Medical Association, 267*(16), 2221-2226.

Ezzy, D. (2002). *Qualitative Analysis, Practice and Innovation*. London, U.K.: Routledge.

FDA. (2002). *Preventable Adverse Drug Reactions:*

A Focus on Drug Interactions. Retrieved 21st March, 2004, from the World Wide Web: http://www.fda.gov/cder/drug/drugReactions/default.htm#Preventing%20Drug%20Interactions

FDA. (2003). *Improving Healthcare through Better Information.* U.S. Food and Drug Administration. Retrieved 2nd Oct, from the World Wide Web: www.fda.gov/oc/mcclellan/strategic_consumer.html

Geyer, S. (2003). Proactive Prevention of ADRs. *Materials Management in Health Care, 12*(5), 36.

Golomb, B. (2002). Letters to the Editor. *Journal of American Medicine Association, 287*(19), 2503.

Grant, E. M., Coulson, R. A. & Wood, S. M. (2000). Adroit and Aegis: An It Solution to the Challenge of Drug Safety Monitoring, Chap. 28. 551-574.

Hamilton, S. (2004). Clinical Decision Making: Thinking Outside the Box. *Emergency Nurse, 12*(6), 18-20.

Hartmann, K., Koller Doser, A. & Kuhn, M. (1999). Postmarketing Safety Information: How Useful Are Spontaneous Reports? *Pharmacoepidemiology and Drug Safety, 8*, s65-s71.

Health Connect (2004). Australian Government Department of Health and Aged Care. Retrieved 3rd April, 2004, from the World Wide Web: www.healthconnect.gov.au

Health Online (2004). Australian Government Department of Health and Aging. Retrieved 3rd April, 2004, from the World Wide Web: www.health.gov.au/healthonline

Holyland, P. W. (2002). *PlanIT: A Multiuser 4D Decision Support Tool for Land and Water Resource Planning.* Paper presented at the First Biennial Meeting of the International Environmental Modelling and Software Society, Manno, Switzerland.

Jarernsiripornkul, N., Krska, J., Capps, P. A., Richards, R. M. & Lee, A. (2002). Patient Reporting of Potential Adverse Drug Reactions: A Methodological Study. *British Journal of Clinical Pharmacology, 53*(3), 318-325.

Jha, A. K., Kuperman, G. J., Rittenberg, E., Teich, J. M. & Bates, D. (2001). Identifying Hospital Admissions Due to Adverse Drug Events Using a Computer-Based Monitor. *Pharmacoepidemiology and drug safety, 10*, 113-119.

Kalachnik, J. E. (1999). Measuring Side Effects of Psychopharmacologic Medication in Individuals with Mental Retardation and Developmental Disabilities. *Mental Retardation and Developmental Disabilities Research Reviews, 5*, 348-359.

Katoh, T., Kinoshita, T. & Shiratori, N. (2000). *Dynamic Properties of Multiagents Based on a Mechanism of Loose Coalition.* Paper presented at the Proceedings of the Third Pacific Rim International Workshop on Multi-Agents.

Kohn, L., Corrigan, J. & Donaldson, M. (1999). *To Err Is Human: Building a Safer Health System.* Washington: Institute of Medicine National Academy Press.

Lachs, M. S. & Boyer, P. (2003). Prevent Medication Mistakes. *Prevention, 55*(3), 187-189.

Lauer, R. H. & Handel, W. H. (1977). *Social Psychology: The Theory and Application of Symbolic Interactionism.* Boston, USA: Houghton Mifflin Company.

Lazarou, J., Pomeranz, B. H. & Corey, P. N. (1998). Incidence of Adverse Drug Reactions in Hospitalized Patients: A Meta-Analysis of Prospective Studies. *JAMA: Journal of American Medical Association, 279(15)*(April), 1200-1205.

Lindquist, M., Edwards, I. R., Bate, A., Fucik, H., Nunes, A. M. & Stahl, M. (1999). From Association to Alert - a Revised Approach to International Signal Analysis. *Pharmacoepidemiology and Drug Safety, 8*, s15-s25.

Macquarie University. (2001). *The Macquarie Dictionary (Online)*. The Macquarie Library Pty Ltd. Retrieved Sept, 2004, from the World Wide Web: www.macquariedictionary.com.au

Mcvea, K. L. S. P., Minier, W. C. & Johnson Palensky, J. E. (2001). Low-Income Women with Early-Stage Breast Cancer: Physician and Patient Decision Making Styles. *Psycho-oncology, 10*, 137-146.

Mead, G. H. (1934). *Mind, Self and Society: From the Standpoint of a Social Behavioralist*. London, UK: The University of Chicago Press.

Medical Director. (2003). *Medical Director*. Retrieved March 2003, from the World Wide Web: http://www.australiandoctor.com.au/md_details.asp

Medlineplus. Retrieved, 2004, from the World Wide Web: http://www.nlm.nih.gov/medlineplus/ency/

Merriam-Webster. (2003). *Merriam-Webster Medical Dictionary*. Retrieved, 2003, from the World Wide Web: http://www2.merriam-webseter.com

Monoharan, T., Taylor, H. & Gardiner, P. (2002). *Collaborative Urban Planner (Cup) - a Multi-User Spatial Decision Support System*. Retrieved Sept 2004, 2004, from the World Wide Web: www.mac.hw.ac.uk/~ceetm2/evaluation/publications/sac2002.pdf

Mussi, S. (1999). Facilitating the Use of Multi-Attribute Utility Theory in Expert Systems: An Aid for Identifying the Right Relative Importance Weights of Attributes. *Expert systems, 16*(2), 87-102.

Myhr, K. (1998). *E-Drug: Adverse Drug Reaction (ADR) Reporting by Patients*. Retrieved, 2004, from the World Wide Web: www.healthnet.org/programs/e-drug-hma/e-drug.199812/msg00040.html

NAPRA. (2003). *Canadian Adverse Event Reporting*. National Association of Pharmacy Regulatory Authorities. Retrieved 6th June, 2003, from the World Wide Web: http://www.drugintel.com/public/canadian_adverse_event_reporting.htm

Naranjo, C. A., Shear, N. H. & Lanctot, K., L. (1992). Advances in the Diagnosis of Adverse Drug Reactions. *Journal of Clinical Pharmacology, 32*, 897-904.

Narayan, S. M., Corcoran-Perry, S., Drew, D., Hoyman, K. & Lewis, M. (2003). Decision Analysis as a Tool to Support an Analytical Pattern-of-Reasoning. *Nursing and Health Sciences, 5*, 229-243.

Norman, T. J., Carbogim, D. V., Krabbe, E. C. W. & Walton, D. (2003). Argument and Multi-Agent Systems. In C. Reed & T. J. Norman (Eds.), *Argumentation Machines: New Frontiers in Argument and Computation* (pp. 15-54). Netherlands: Kluwer Academic Publishers.

NPS. (2004). *Medicines Line*. National Prescribing Service Limited. Retrieved August, 2004, from the World Wide Web: www.nps.org.au

O'Brien, M. C. (2001). *Final Report to Department of Health and Aged Care for Contract for Services GPCG #12. Adverse Drug Reactions Improved Decision Support (ADRIDS)*. Collaborative Centre for E-Health. Retrieved Aug, 2002, from the World Wide Web: http://www.gpcg.org/publications/docs/projects2001/GPCG_Project12_01.PDF

O'Brien, M. C. & Yearwood, J. L. (2002). *Insights into Consumer/Doctor Decisions Surrounding Adverse Drug Reactions and Prescribing*. University of Ballarat. Retrieved Mar, 2003, from the World Wide Web: http://www.ballarat.edu.au/ard/itms/publications/researchPapers/Papers_2002/02-19.pdf

O'Brien, M. C. & Yearwood, J. L. (2003). *Insights into Consumer Decisions Surrounding Adverse Drug Reactions: Some Preliminary Results*. Paper presented at the Combined Conferences of the Eleventh National Health Informatics Conference, Applying Socio-technical Practices and Principles, and the Twelfth National RACGP Computer Conference, Beyond the Box: Making IT work for GP's and Patients., Sydney, Australia.

O'Brien, M. C. & Yearwood, J. L. (2004). *Risk: Drug Therapy Versus Adverse Drug Reaction. A Case Study Approach with Consumer, Medical and Expert Views*. Paper presented at the 12th Health Informatics Conference: Let's Make a Difference with Health ICT, Brisbane, Australia.

O'Brien, M. C. & Yearwood, J. L. (2005). Decisions Surrounding Adverse Drug Reaction Prescribing: Insights from Consumers and Implications for Decision Support. *Journal of Research and Practice in Information Technology, 37*(1), 57-71.

O'Neill, E. S., Dluhy, N. M. & Chin, E. (2005). Modelling Novice Clinical Reasoning for a Computerized Decision Support System. *Journal of Advanced Nursing, 49*(1), 68-77.

Orsini, M. & Funk, P. A. (1995). An ADR Surveillance Program: Increasing Quality, Number of Incidence Reports. *Formulary, 30*(8), 454-461.

Payne, T. H., Savarina, J., Marshall, R. & Hoey, C. T. (2000). *Use of a Clinical Event Monitor to Prevent and Detect Medication Errors*. Retrieved Feb 2002, from the World Wide Web: http://www.amia.org/pubs/symposia/D200317.PDF

Phillips, S. (2002). *Report of the Electronic Decision Support Governance Workshop*. Melbourne: National Institute of Clinical Studies.

Pirmohamed, M., Breckenridge, A. M., Kitteringham, N. R. & Park, B. K. (1998). Fortnightly Review: Adverse Drug Reactions. *British Medical Journal, 316(7140)*(April), 1295-1298.

Purcell, P. (2001). *Presentation: Adverse Drug Reactions*, University of Ballarat.

Purcell, P. (2003). Personal Communication with Dr. Purcell. Victoria, Australia.

QSR. (2002). *QSR NVivo (Version 2.0.161)*: QSR International Pty. Ltd.

Raschke, R. A., Gollihare, B., Wunderlich, T. A., Guidry, J. R., Leibowitz, A. I., Peirce, J. C., Lemelson, L., Heisler, M. A. & Susong, C. (1998). A Computer Alert System to Prevent Injury from Adverse Drug Events - Development and Evaluation in a Community Teaching Hospital. *JAMA: Journal of American Medical Association, 280*(15), 1317-1320.

Richards, D., Boettger, K. & Britt Fure, A. (2002). *Using RECOCASE to Compare Use Cases from Multiple Viewpoints*. Paper presented at the Enabling Organisations and Society through Information Systems: ACIS 2002, Victoria University, Melbourne Australia.

Roughead, L. & Semple, S. (2002). *The Second National Report on Patient Safety: Improving Medication Safety*: Safety and Quality Council.

Safety and Quality Council. (2003). *Alerts*. Retrieved 10th November, 2003, from the World Wide Web: www.safetyandquality.org/links_alerts.cfm

SCHIN. (1998). *Prodigy Project: Computerisation in GP Practices. 1996 Survey*. Newcastle, U.K.: Sowerby Centre for Health Informatics at Newcastle.

Scott, G. C. & Lenert, L. A. (2000). *What Is the Next Step in Patient Decision Support?* Paper presented at the Proceedings AMIA Symposium.

Smith, M. K. (2001). *Donald Schon: Learning Reflection and Change*. Infed. Retrieved March, 2005, from the World Wide Web:

Stevenson, F. A., Barry, C. A., Britten, N., Barber, N. & Bradley, C. P. (2000). Doctor-Patient Communication About Drugs: The Evidence for Shared Decision-Making. *Social Science and Medicine, 50*(6), 829-840.

Stewart, M. A., Brown, J. B., Donner, A., McWhinney, I. R., Oates, J., Weston, W. W. & Jordan, J. (2000). The Impact of Patient-Centred Care on Patient Outcomes. *Journal of Family Practice, 49*(9), 796-804.

Stewart, M. A., Meredith, L., Brown, J. B. & Galajda, J. (2000). The Influence of Older Patient-Physician Communication on Health and Health-Related Outcomes. *Clinics In Geriatric Medicine, 16*(1), 25-36.

Strauss, A. & Corbin, J. (1998). *Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory*. (2nd ed.). Thousand Oakes, California: Sage.

Sutcliff, H., McMorran, M. & Morawiecka, I. (2000). Canadian Adverse Drug Reaction Newsletter. *CMAJ: Canadian Medical Association Journal, 162*(7), 1044-1047.

Sykes, J. B. (1976). *The Concise Oxford Dictionary of Current English*. Oxford: Oxford University Press.

Taylor, C. (2000). Clinical Problem-Solving in Nursing: Insights from the Literature. *Journal of Advanced Nursing, 31*(4), 842-849.

TGA. (2003). *Adverse Drug Reactions: Frequently Asked Questions*. Retrieved 6th June, 2003, from the World Wide Web: http://www.health.gov.au/tga/adr/adrfaq.htm#who

Thomas, K. W., Dayton, C. S. & Peter, M. W. (1999). Evaluation of Internet-Based Clinical Decision Support. *Journal of Medical Internet Research*.

Towle, A. & Godolphin, W. (1999). Framework for Teaching and Learning Informed Shared Decision Making. *British Journal of Medicine, 319*(18 September), 766-769.

Tuominen, K., Talja, S. & Savolainen, R. (2003). Multiperspective Digital Libraries: The Implications of Constructionism for the Development of Digital Libraries. *Journal of the American Society for Information Science and Technology, 54*(6), 561-569.

VDUAC. (1999). *Adverse Drug Reaction Reporting*. Victorian Drug Usage Advisory Committee. Retrieved March, 2005, from the World Wide Web: www.vduac.org.au/adrs.doc

VDUAC. (2002). *Beyond Blame: Exploring Practical Approaches to the Control of Adverse Drug Events*. Melbourne: Victorian Drug Usage Advisory Committee on Drug Error Prevention in Victorian Hospitals.

WHO. (2002). *Safety of Medicines: A Guide to Detecting and Reporting Adverse Drug Reactions: Why Health Professionals Need to Take Action*. World Health Organisation. Retrieved March, 2005, from the World Wide Web: http://www.who.int/medicines/library/qsm/who-edm-qsm-2002-2/esd_safety.pdf

WHO. (2003). *Who Programme*. Retrieved 22nd March, 2003, from the World Wide Web: http://www.who-umc.org/whoprog.html

WHO. (2004, 19/7/04). *Who Collaborating Centre for International Drug Monitoring*. Uppsala monitoring centre. Retrieved 1/8/04, 2004, from the World Wide Web: http://www.who-umc.org/umc.html

Yin, R. (2003). *Case Study Research: Design and Methods* (3rd ed. Vol. 5). Thousand Oakes, California: Sage Publications Inc.