Can the Heinrich ratio be used to predict harm from medication errors?

Report to the Patient Safety Research Programme (Policy Research Programme of the Department of Health)

Dr. Katja Taxis
Assistant Professor of Clinical Pharmacy and Pharmacotherapy Department of Pharmacotherapy and Pharmaceutical Care, University of Groningen, The Netherlands

Prof. Steve Gallivan
Director, Clinical Operational Research Unit, Department of Mathematics, University College London

Prof. Nick Barber
Professor of the Practice of Pharmacy, Head of Department of Practice and Policy, The School of Pharmacy, University of London

Prof. Bryony Dean Franklin
Director, Academic Pharmacy Unit, Hammersmith Hospitals NHS Trust & Visiting Professor, Department of Practice and Policy, The School of Pharmacy, University of London

Competing interest of authors: None

Correspondence to:

Prof. Nick Barber
Department of Practice and Policy
School of Pharmacy
Mezzanine Floor, BMA House
Tavistock Square
London WC1H 9JP

Tel: 020 7874 1270
Email: n.barber@pharmacy.ac.uk

September 2005

Contents

List of Figures

List of Tables

.

.List of Abbreviations

ADE: Adverse drug event

ADR: Adverse drug reaction

A&E: Accident and Emergency Unit

CI: Confidence Interval

ICD9: International Classification of Diseases, version 9

MHRA: Medicines and Healthcare products Regulatory Agency

NCCMERP: National Coordinating Council for Medication Error Reporting and
Prevention

NPSA: National Patient Safety Agency

T: Equilateral triangle

Executive Summary

The Heinrich ratio is widely used in health and safety work; it relates the number of accidents that do not result in harm to the number that result in minor harm, and the number resulting in major harm. Typically this is written as a ratio based on 1 case of major harm, for example 300:29:1.

The purpose of this study was to establish whether, for medication errors, there exists a fixed Heinrich ratio between the number of incidents which did not result in harm, the number that caused minor harm, and the number that caused serious harm. If this were the case then it would be very useful in estimating any changes in harm following an intervention. Serious harm resulting from medication errors is relatively rare, so it can take a great deal of time and resource to detect a significant change. If the Heinrich ratio exists for medication errors, then it would be possible, and far easier, to measure the much more frequent number of incidents that did not result in harm and the extent to which they changed following an intervention; any reduction in harm could be extrapolated from this.

We formalised the properties the Heinrich ratio would require if it was to be used in the desired way: the ratio would have to be stable for medication errors; we would need to know its values; any change in one number must be associated with a proportional change in the two others; there would have to be a way of constructing Confidence Intervals around the ratio so statistical significance of a change could be tested; finally, it would be preferable if it could be represented graphically to aid communication and understanding. We tested whether these properties existed by a combination of approaches which included logic, mathematical modelling and reviewing the literature. These approaches are underpinned by Appendix 3, which contains a substantial commentary on medication error definitions, research methods and ways of assessing the severity of a medication error.

Using barycentric coordinates, the three numbers in the Heinrich ratio were plotted as a point on an equilateral triangle. A formula was developed which allowed the estimation of a 95% confidence region around the point. Hence it is now possible to compare two Heinrich ratios and establish whether they are significantly different. This has not been possible before. (Chapter 4, Appendix 1, Appendix 2)

A review of Heinrich's original research raised significant doubts about its validity in complex areas such as medication error. (Chapter 2)

Logic showed that, while situations could be envisaged in which the Heinrich ratio remained stable after an intervention, equally there could be situations in which two of the numbers changed but the third did not. (Chapter 3)

Mathematical modelling showed the ratio would be exquisitely sensitive to the definitions used (no harm accidents, minor harm, major harm). Depending on the definitions, virtually any ratio could exist. The literature review showed the definitions used in the literature are widely different. (Chapter 3 and Appendix 3)

Heinrich ratios were created using data from existing papers on harm resulting from medication errors. The resulting ratios were very different. (Chapter 5)

The lack of a stable Heinrich ratio for medication errors could have been due to the variations between definitions. We therefore explored two other sources of health data in which there are well defined definitions: outcomes following A&E admissions, and road traffic accidents. In neither case were stable ratios found. (Chapters 4 and 6)

In summary, we found no evidence to support a stable Heinrich ratio for medication errors. However, establishing a relationship between medication errors and harm is extremely important. We make some preliminary suggestions about the relationship in Chapter 7 and recommend the following research agenda:

There is an urgent need for a common taxonomy in medication error research for defining, classifying, measuring and reporting medication incidents. Journal editors need to be involved. We envisage some form of consensus statement, such as the CONSORT statement for clinical trials.

The relationship between errors and harm needs to be better understood. Our work suggests that a simple "linear form" (halve the errors and you halve the harm) is probably not a reasonable supposition. This would benefit from further study and, as the current report shows, a multidisciplinary approach to such investigation would seem most beneficial.

A risk model needs to be built relating medication error to harm. *(word count 730)*

1 Background

This project started in one place and ended, unexpectedly, in another. We start by explaining this change in direction. The research brief was to develop a consensus statement on a classification of the severity of medication errors. Medication errors are one of the most frequent, and severe, examples of medical error.[1;2] They are important in their own right, and also in that they can provide generalisable lessons for other types of medical error.

We had planned to use a typical process of literature review, followed by presentations by experts to a multidisciplinary quasi-judicial panel, which would then synthesise the final definitions. Definitions need to allow the right amount of discrimination to serve a specific purpose. In order to understand the purpose for which the definitions would be used, we were asked to meet with Professor David Cousins, Head of Medication Safety at the National Patient Safety Agency (NPSA). From this meeting the origin of the research brief was clarified as follows:

The NPSA wishes to use a learning organisation approach, in combination with central initiatives, to create a safer NHS for patients by reducing accidental harm. To do this it set up a scheme to report and monitor errors. Error is a much more frequent event than harm. Given that any reporting system is only likely to detect a small proportion of the number of real events, and that harm is rarer than error, it can be difficult to demonstrate a reduction in harm following any successful initiative. This need not be a problem if there is a direct relationship between the number of errors and the number of harmful events. Such a relationship is described by the Heinrich ratio (usually called the Heinrich triangle), first described in 1931.[3] For every case of serious harm, it relates the number of cases of minor harm that occur, and the number of cases of erroneous acts that did not result in harm. This ratio is used widely in the risk management industry, and is routinely shown in UK health and safety documents and reports on incidents.
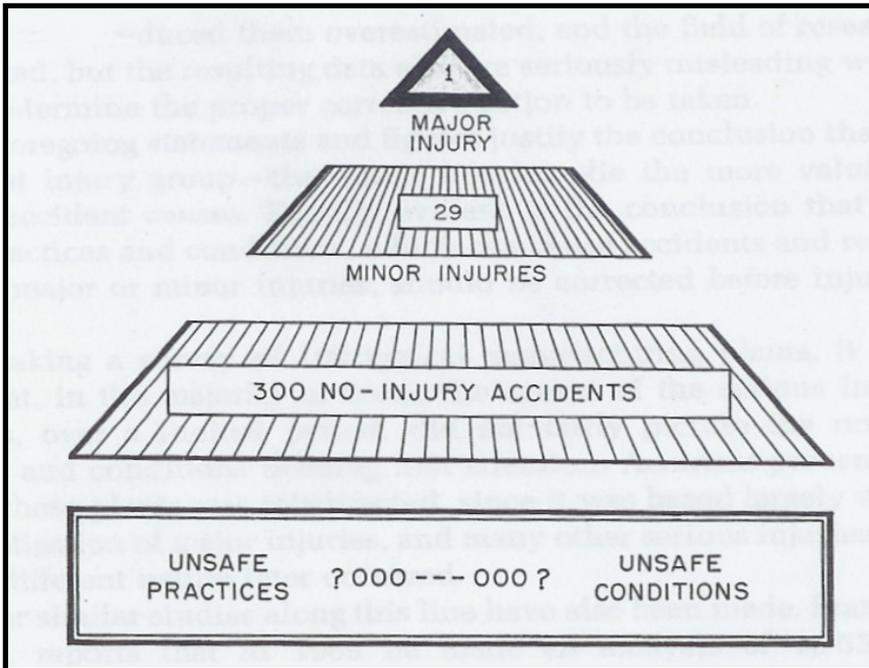
Figure 1: The Heinrich triangle (from Heinrich's original publication[3])

The thinking of the NPSA, in line with Health and Safety Executive thinking, was that, if error and severity of harm could be related for a medication incident then, in future, in line with the Heinrich triangle definitions, the effectiveness of any intervention could be assessed. Medication errors are reported to the NPSA. If we could show medication errors were reduced by n%, then we could predict harm had also been reduced by n%. This thinking led to the original request to create definitions for the severity of errors. In order to construct the Heinrich triangle to link medication errors to harm it would be necessary to define the equivalents of "no injury accidents", "minor injury" and "major injury".

The request seemed very reasonable, however, knowing how the definitions of severity would be used, we decided to formalise the questions that must be answered for the Heinrich triangle to deliver the required information. These were:

1. Is there a Heinrich triangle (ie stable ratio) relating major and minor harm to medication errors?
2. What are the values in the ratio (errors that do not cause harm: minor harm: major harm)?
3. Is any change linearly proportional? For example, if the number of errors overall is reduced by 20%, will minor harm and major harm also be reduced by 20%?

4. How could the Heinrich ratio be represented graphically to illustrate and communicate change?

5. How could we show that any change was statistically significant, and not the result of chance? For example, is 247:28:1 significantly different to 312:25:1?

In order to explore these questions we have investigated the issue using three different approaches:

1. logic
2. mathematical modelling
3. data from the literature - empirical evidence

The following report explains each of these approaches, and answers the fundamental questions, posed above, about the Heinrich triangle.

We begin in Chapter 2 with a summary of the concept of the Heinrich triangle based on the original literature. We then review how the concept is understood by examining its usage in various fields, particularly focusing on medicine. Furthermore, this chapter raises questions about the validity and generalisability of the concept based on information in the literature.

The logical and mathematical basis of the Heinrich triangle is examined in Chapter 3. Exemplar vignettes, based on mathematical insight, are constructed to explore situations in which the Heinrich triangle may be valid and situations in which there is clearly no basis for the concept.

The next chapters of the report examine the empirical evidence of the Heinrich triangle. We investigate the concept using data from published medication error studies and from road traffic accidents. However, it was first necessary to develop a new graphical method to display data of three categories (minor, moderate, severe events) including the construction of confidence regions to allow statistical comparisons of different ratios (Chapter 4). The usage of this method is also illustrated in Chapter 4 using published data from public health.

In Chapter 5 we display data from published medication error studies to investigate if there is a Heinrich ratio for medication errors. However, a major limitation of using

existing data for such an attempt is the lack of standardisation in defining medication errors, data collection methods and assessment of harm from medication errors. We include more detailed information about these issues in Appendix 3. Further insight into using Heinrich's concept was gained by analysing data from road traffic accidents (Chapter 6).

We conclude the report with a final discussion answering the research questions posed above (Chapter 7).

2 A review of the original concept of the "Heinrich Triangle" and its application in medicine

In this section we review the original literature on the Heinrich triangle from the 1930s and the claims for the concept. We then explore how the concept is understood by examining its usage in various fields, particularly focusing on medicine. Furthermore, this chapter raises questions about the validity and generalisability of the concept based on information in the literature.

2.1 The original concept of the "Heinrich triangle"

H.W. Heinrich (1881-1962) was an engineer working for an insurance company in the United States. He was interested in ways to reduce the number of insurance claims. For this purpose he studied accident records. This work resulted in the publication of his book "Industrial accident prevention" in 1931. This was so successful that subsequently further revised editions were published, some of them with other co-authors. The last (fourth) edition was published after his death in 1980. The book outlines why industrial accidents occur and how these could be prevented. Ideas and models are mainly based on the analysis of thousands of closed-claim-file insurance records of industrial accidents and company records. In the following we focus on a concept presented in the chapter "Basic philosophy of accident prevention" which has consequently become known as the "Heinrich triangle" or "Heinrich ratio".

The Heinrich ratio is based on the observation that accidents which resulted in a serious injury or death of the employee were often preceded by similar accidents which, often only by chance, did not result in injury. Heinrich's systematic analysis of more than 50,000 cases of accidents at work taken from company records from the 1920s showed that on average 1 major injury was preceded by 29 minor injuries and 300 no-injury accidents.[3] Table 1 shows examples of the cases, illustrating their very varied nature and ratios.

1. An employee took a (forbidden) short cut on his way to work, crossing a fence and railroad tracks every day for two and a half years (5000 times). One day he was seriously injured by an engine which he had overlooked because of a car which blocked his vision. It was estimated that he had narrowly escaped injury approximately 500 times and had minor injuries about 38 times before his major injury. The ratio was therefore 500 – 38 – 1.
2. A circular saw operator lost his thumb when, in violation of instructions, he pushed the board past the saw with his fingers instead of using a push stick. It was estimated that he had operated the machine in a similar way over 1500 times. During this period he had sustained many minor cuts and hundreds of 'close shaves'. Estimated ratio: 350 – 40 – 1.
3. A mill employee slipped and fell on a wet floor and fractured his kneecap. For more than six years it had been the practice to wet down too great an area of floor space at one time and to delay unnecessarily the process of wiping up. Slipping on the part of one or more employees was a daily occurrence. The ratio of non-injury slips to the injury was 1800 to 1. Estimated ratio was therefore 1800 – 1 – 0.

Table 1: Three cases to illustrate how the Heinrich triangle was established [3]

The overall message was that accident investigation should include the analysis of no-injury accidents. Since there are many more no-injury accidents than major injuries, this provides a larger data base for accident investigations. Furthermore, accidents causing major injuries were often isolated events which did not give all the information needed to prevent similar accidents. Just studying major injury accidents would therefore have limited effect. This was substantiated with an analysis of 100 industrial plants where accident prevention work was focused on investigating major injuries. It was found that despite accident prevention efforts, serious injuries still occurred, because they were of a slightly different nature to the initial accidents.

Another important conclusion that Heinrich drew from his work was that reducing the number of no-injury accidents was going to reduce the number of major injuries proportionally, because the frequency of major injuries varied directly with the frequency of no-injuries accidents. This also meant that corrective measures could be implemented even before a serious accident occurred. In summary, the three main statements underlying Heinrich's triangle are summarised in Table 2.

- There is a stable ratio of minor (no injury) to moderate to major injuries following accidents
- The investigation of minor/no-injury accidents provides valuable information to prevent further accidents
- Changes in the frequency of minor injuries cause a proportional change in harm

Table 2: The concept of the Heinrich triangle [3]

As is common for empirical work at the time, little detail is provided about methods for data collection and analysis which makes it difficult to judge the scientific base of this work by current standards. Nevertheless, the concept has been very influential and, as the following section shows, is referred to nearly 75 years after the first edition of the book.

2.2 The use of the concept of the "Heinrich triangle"

Using a similar approach "Heinrich ratios" have been established in other areas of health and safety and some examples have been summarised in Table 3. For example, one that is also widely referred to has been published by Bird and Germain.[4] They argued that no-injury accidents most often involved property damage. For each disabling injury they found 500 cases of property damage. So reducing property damage will also result in a reduction in disabling injuries. The concept is also used by the Health and Safety Executive in the UK, for example in monitoring the safety of oil tankers [5] or in investigating the cost of accidents at work.[6] It has even been used to compare injury rates of professional footballers with rates in other areas (concluding that professional footballers do not have higher injury rates than people working in other areas [7;8]).

Heinrich's findings have also been used frequently to justify establishing near miss reporting systems. In this context, Heinrich's term of no-injury accidents is replaced by the term "near miss" referring to an incident which did not result in a harmful injury, for example by the Department of Transportation in the USA or the chemical industry.[9] Table 4 includes some quotes taken from the papers to show how the concept is understood. Many authors state that investigating "near misses" provides valuable data *and* that there is a proportional relationship between near miss events and major accidents, i.e. reduction in the number of near miss events will reduce the number of harmful accidents.

Country, year, reference	Details
	Heinrich ratios which show the frequency of incidents with different outcomes
USA 1966: Property damage [4]	Re-interprets the non-injury accidents as accidents which often involve property damage. To reduce property damage these incidents need to be investigated. Established a ratio of disabling injury : minor injuries : property damage accidents as 1:100:500 based on 90 000 incidents spanning a 7 year period in a steel production company.
USA 1996: Property damage and injuries at work [10]	An analysis of 1 753 498 accidents reported by 297 companies (21 industrial groups) to an insurance company gave a ratio of 1 serious or major injury : 10 minor injuries : 30 property damage accidents : 600 incidents with no visible injury or damage.
	Establishing Heinrich ratios to monitor safety performance
UK, 1993: Cost of accidents at work [6]	Heinrich ratios are established to investigate the cost of accidents at work
2003, UK: Safety of oil tankers [5]	Heinrich ratios are established for reported incidents with tankers. The data are used to monitor changes in tanker incidents over time.
1996/1998, UK: Accident rates of professional football players [7;8]	Heinrich ratios are established to compare the accident rates of professional football players across different football leagues (premier league versus first division) and with other professions.

Table 3: The use of the Heinrich triangle in various fields

Country, year, reference	Details
Germany, 2004: Government accident investigation in environmental affairs [11]	"Lessons can be learnt from non-notifiable accidents as well as from accident notifiable due to German Regulation on Major Accidents and are independent from the consequences of the accidents. There are no fundamental differences in the causes of major or minor events too."
Norway, 1999: Near miss reporting in industry [9]	Accident and near miss reporting data from a Norwegian oil and aluminium company showed an inverse correlation between the number of reported near misses and the number of accidents. The more near miss reports there were, the lower the number of accidents. Therefore it was concluded that the number of near miss reports was a good measure of the safety culture of the industry. "Focusing on reduction of actual near miss occurrences will reduce frequency of accidents." "Iceberg concept".
USA, 2004: Department of Transportation [12]	Department of Transportation (USA) Bureau of Transportation Statistics using Heinrich's work to justify investigation of near miss accidents
Canada 2001, Canadian Safety Council [13]	"The bottom line is that it pays to reduce the frequency and severity of minor collisions. Companies that take preventive action on minor, non-injury incidents have fewer collisions with minor injuries, and fewer major crashes with severe injuries."
USA, 2003: Near miss incident management in the chemical industry [14]	"In review of adverse incidents in the process industries, it is observed, and has become accepted, that for every serious accident, a larger number of incidents result in limited impact and an even larger number of incidents result in no loss or damage. This observation is captured in the well known safety pyramid."

Table 4: The use of the Heinrich triangle to justify near miss reporting

As has been already highlighted, Heinrich's concept is also used in medicine. Table 5 summarises examples. Most of these use the concept to justify the use of near miss reporting systems. For example, in the UK, a national error reporting system has been established. Error reports will be used to find the general defects in the system.[15] Individuals are encouraged to report not only errors which resulted in serious harm to the patient, but also potential errors or so called "near misses". It is suggested that analysis and learning from near misses or no-harm accidents can help prevent serious injuries.[15] Because medication errors are recognised to be unacceptably common this concept has been particularly promoted in this area.[16]

Author and title of publication	Quotes from publication
Bion and Heffner (2004), Challenges in the care of the acute ill [18]	"If the Heinrich ratio can be applied to health care the near-miss data or latent failures provide a tremendous opportunity to improve patient safety"
Furukawa et al. (2003) Voluntary medication error reporting program in a national Japanese University hospital [19]	"According to the well-known Heinrich ratio, there is always a large number of similar errors that were able to be prevented for each case of an error that produces serious consequences."
Kaplan (2001) Lessons learned [20]	"Similarly, no-harm events provide a rich source of information. A consistently observed ratio of 300:1 no-harm events (including near misses) to adverse events has been found in a wide range of industries."
Meyer et al. (1999) Error reporting systems [21]	"Reporting systems can be evaluated on the proportion of minor to more serious incidents reported; for every major injury, there are 29 minor injuries and 300 non-injury accidents."

Table 5: Quotations from reports/papers to illustrate how the Heinrich triangle is referred to in the medical field to justify near-miss reporting or investigation of near-miss data

The concept has been also used to prioritise where to focus resources and services in accident and emergency departments in the USA.[21] The frequency of accidents were displayed as a ratio of accidents which result in death, hospital admission or emergency department visits (taken from ecodes based on ICD9 classification). Figure 2 is an example of how the data were displayed. Ratios were compared across different types of injuries, for example firearms injuries and falls. Data were used to prioritise injury control efforts and possibly to target approaches to injury prevention and identify successful preventive efforts/interventions. It is noteworthy that in this paper a wide range of different ratios were found. Consequently, the shapes of the graphs deviate from the "classical" triangle. For example, the usage of firearms in suicide attempts results more often in death than in hospital admission or emergency department visits (Figure 3). High fatality ratios can therefore result in an inverted triangle.
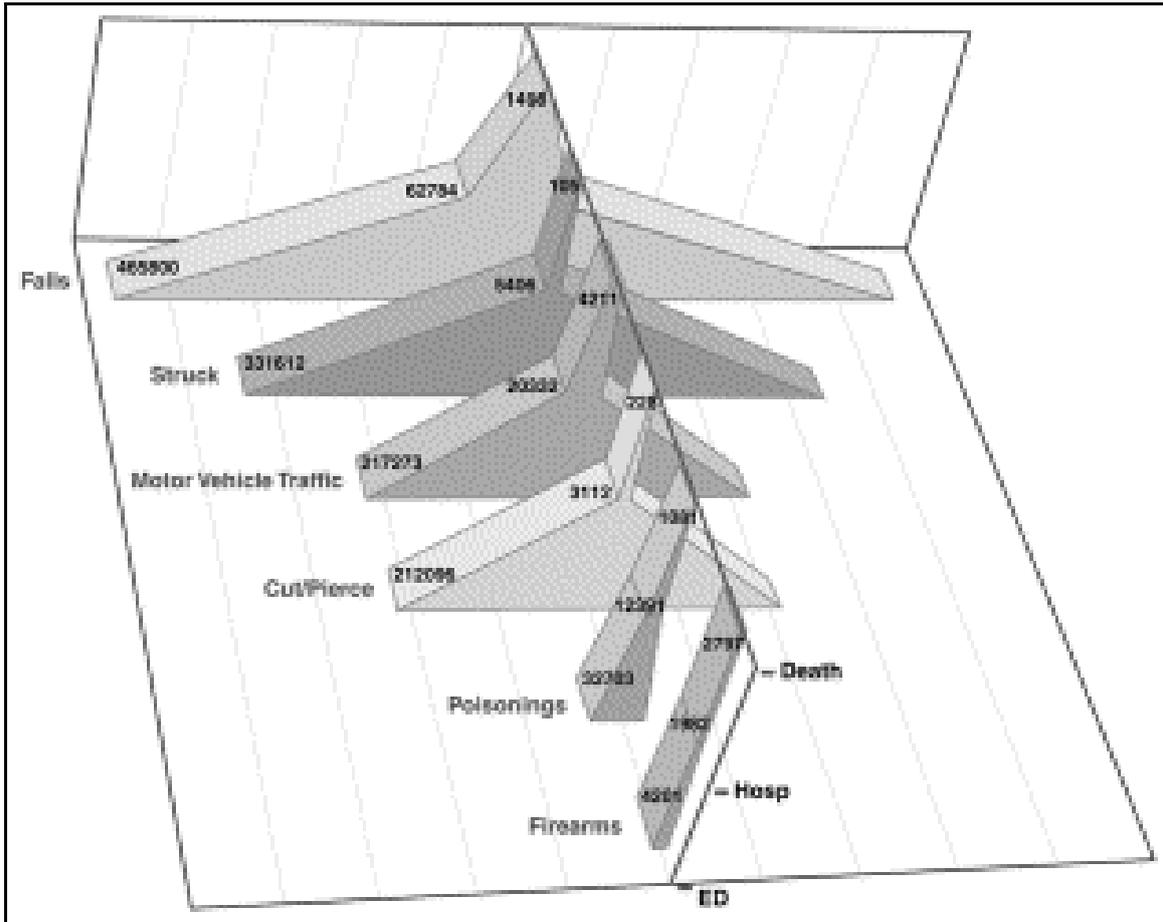
Figure 2: Ratio of different types of accidents by outcome (death, hospital admission or emergency department visits) taken from ecodes based on ICD9 classification [21] (awaiting copyright to reproduce this figure)
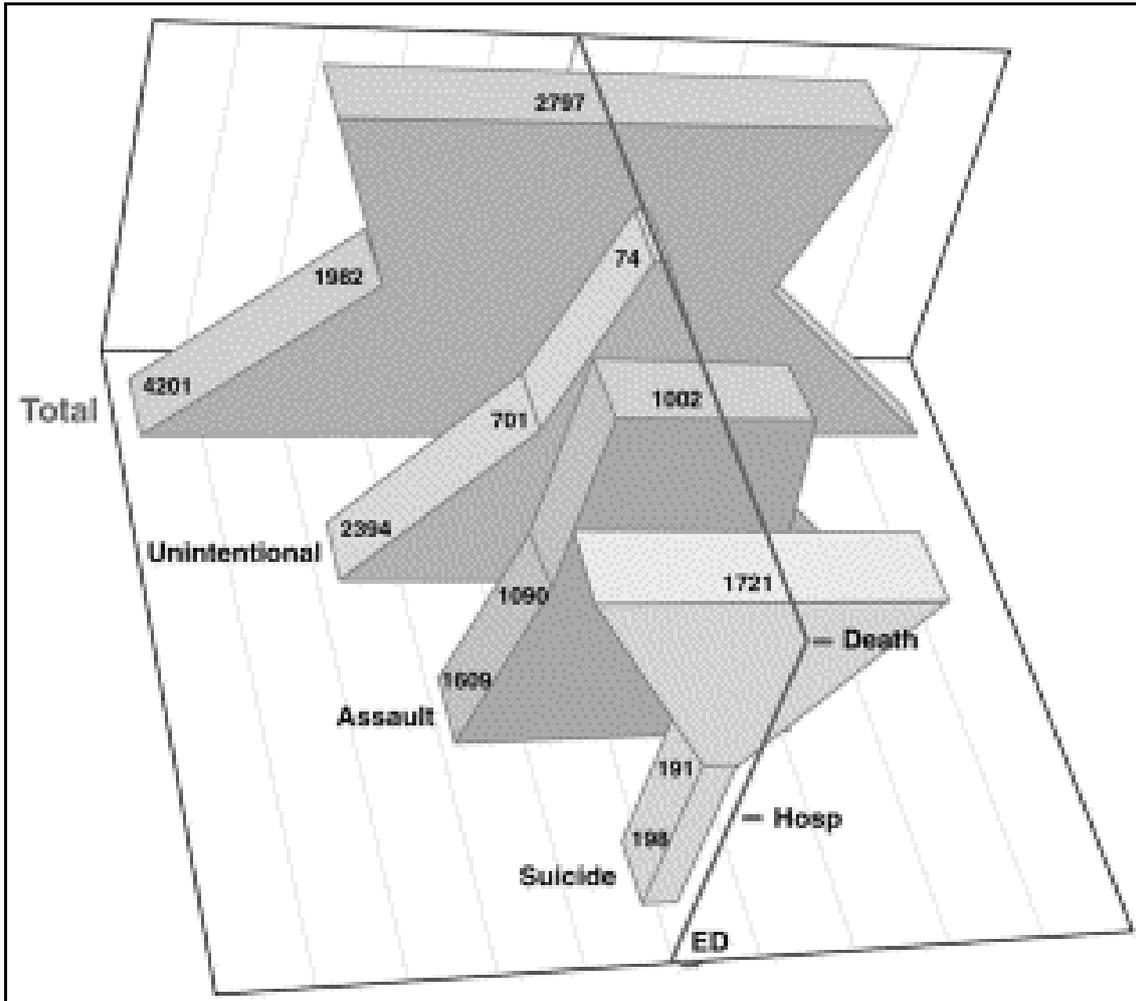
Figure 3: Ratios of accidents involving firearms due to different causes (unintentional, assault, suicide) [21] **(awaiting copyright to reproduce this figure)**

2.3 Validity and generalisability of the Heinrich triangle

As we have shown, the concept of the Heinrich triangle [3] has been used widely, but little work has been done to test its validity and generalisability by current scientific standards. In this respect it is useful to critically review the methods and data used in the original work of Heinrich.

Two main concerns arise about the methods. First, the cases were a random sample of insurance files. This is likely to be a selected sample of cases with a major outcome, as only cases involving considerable (personal) damage were likely to be reported to the insurance company. Cases would not be reported if they were not covered by the insurance policy. Second, as with any document analysis, the data that Heinrich used were created not for research purposes or accident investigation, but for insurance

claims.[22] Therefore, it remains unknown to what extent they represent "true" accounts of the accidents.

A closer review of the characteristics of the cases indicates more restrictions to the possible generalisability of the conclusions. The cases as presented in Heinrich's book [3] refer to:

- industrial processes and practices of the 1920s involving relatively simple manual tasks.
- individuals deliberately deviating from known safety procedures (violations), such as not using the safety tools provided when operating the circular saw, or smoking while refueling.
- (failed) action or performance of one individual in one task over time. Examples include one worker crossing the railway tracks at a forbidden place for years, being slightly injured a few times and badly injured once, and the case of one employee of a filling station who regularly smoked during fueling until the time he caused a bus to explode, killing many passengers.

Reviewing these characteristics raises questions as to whether Heinrich's concept applies to modern industry which involves complex processes in which accidents are likely to involve many different operators and technologies. The concept may also not refer to other types of errors (eg not knowing how to carry out certain tasks instead of deliberately violating existing guidelines).[23] This is of particular concern as it has been shown recently that most prescribing errors involve mistakes (defined using Reason's terminology [23] of differentiating unintentional human errors as mistakes, slips and lapses. Mistakes in this context were that staff thought, incorrectly, they were doing the right thing).[24] Only certain types of medication errors may be related to violations, such as the too rapid administration of bolus doses of intravenous drugs.[25]

Another issue has been raised by Wright and van der Schaaf [26] recently. For cases with the above listed characteristics it may be assumed that the accidents leading to minor/no injuries have the same causes as the major injuries (as they mostly involve one individual repeating the same task). This is referred to as the "common cause hypothesis". Wright and van der Schaaf [26] found that Heinrich's concept has been frequently misunderstood, because studies failed to show that serious accidents had

similar causes to minor accidents. In many studies, it was assumed that finding a ratio close to the original Heinrich ratio would be sufficient to assume that consequently the frequency of major injuries could be reduced by removing causes of no-injury injury accidents. Wright and van der Schaaf [26] state that, to use Heinrich's ratio in a given area, the common cause hypothesis has to be validated using accident or injury data which has been analysed for causes contributing to the incidents and not only on the frequency of accident severity. Their analysis of causal patterns from data from the UK railway industry suggested common causes contributing to minor and major accidents which would confirm Heinrich's concept in that setting.

There is some recognition of the importance of "common cause" in Heinrich's books. The first edition contained data to show that major injuries and minor or no-injuries had common causes; this was omitted in further editions. The last edition of the "Heinrich" book in 1980 [27] even discusses an example in which Heinrich's concept does not apply. Data from the National Safety Council of the USA shows that, although the overall number of accidents had decreased, the number of accidents that caused disabilities had not decreased to the same extent over the years (not expected according to the concept). It suggested that the circumstances (and causes) surrounding severe accidents were different from minor injuries. In such cases the focus of accident prevention efforts should predict the areas of most serious injuries and try and prevent them.

Reviewing the literature on medication errors, there is little evidence that medication errors with minor outcomes follow similar causal patterns to serious medication errors. Firstly, because few studies have formally assessed causal patterns of medication errors and none have analysed their data on causes by (potential) outcome. Secondly (and more importantly) we find many examples where errors involving certain medicines have little capacity to cause major injury (e.g., administration of one instead of two vitamin tablets on one occasion) and in contrast certain medicines if involved in an error will almost always have major clinical consequences (e.g., intrathecal instead of intravenous administration of vincristine or the repeated daily instead of weekly administration of methotrexate).

Another point of weakness in the argument for the Heinrich triangle is that there is no discussion of variability. It is easy to calculate an average, but not necessarily

meaningful. The ratios that are calculated for the first two cases shown in Table 1 are close to the average ratio of 1:29:300, in contrast, case number three has a ratio of 0:1:1800. There may be cases in which an accident may often result in a major injury, such as falling from a great height. Even later work and adaptations of the Heinrich ratios do not include statistical considerations of confidence intervals around the ratio. This is particularly important if one wants to use the Heinrich ratio to determine a reduction in the number of accidents. When should a reduction be considered significant? We are not aware of anyone attempting a statistical analysis of a difference between Heinrich ratios.

Finally, the classification into three distinct categories is also an issue. For example, Heinrich does not provide any definitions of how he differentiated between moderate and major injuries. This will clearly have an impact on the ratio.

2.4 Summary

Reviewing the original literature on the Heinrich ratio and its application in various fields, we find three "commonly held beliefs".

- There is a stable ratio of minor to moderate to major injuries following accidents
- The investigation of minor/no-injury accidents provides valuable information to prevent further accidents
- Changes in the frequency of minor injuries cause a proportional change in harm

Reviewing the medical literature in the area we find that there is a general belief that all three statements apply in medicine and we presented examples how the Heinrich ratio is used in public health. An in-depth review of methods used to establish the original ratio raises serious doubts about the validity and generalisability of the concept. With the exception of recent attempts in the railway industry, these questions have been rarely addressed.

In the next chapter we will examine the logical and mathematical basis of the Heinrich triangle.

3 Cautionary tales concerning the Heinrich triangle in relation to patient safety – thought experiments by a mathematician

3.1 Introduction

Here, we discuss the face validity of the Heinrich's triangle concept viewed from a logical perspective. In simple terms, Heinrich's work has been used to suggest that if system changes are introduced that reduce the frequency of "no-harm" incidents, then the frequency of "minor" and "major" incidents should also decrease. In stronger terms, it has also been suggested that the three type of incident occur with a fixed relative frequency. If this were the case, then observing the effects of a given remedial action on "no-harm" errors would allow one to estimate the overall reduction in minor and major incidents; clearly useful since the infrequency of the latter means that large scale data collection would be required before direct evaluation of new safety procedures could be carried out. However, merely being useful does not make a proposition the case. Here we examine whether the extent to which the notions of the Heinrich triangle are reasonable and the potential pitfalls of putting too much faith in the concept.

The discussion is based on the use of deductive reasoning and involves adopting the role of devil's advocate, constructing exemplar vignettes, based on mathematical insight, to illustrate potential problems that might arise if too much faith is put in the Heinrich triangle notions.

3.2 The rationale behind using the devil's advocate role to provide constructive criticism

The use of mathematical modelling is relatively uncommon in relation to health services research and some of the techniques used may be somewhat alien to those concerned with patient safety. This is particularly the case in relation to the present discussion, since it is based on little more than thought experiments. There has not been the opportunity to collect data to confirm or deny whether the examples constructed are typical or atypical.

There are those who may feel uneasy with the notion of study methods that are devoid of any data. In view of this, it is perhaps worth promoting the use of exemplar vignettes for identifying potential system problems. The method is basically concerned with constructing counterexamples, a technique that is used frequently in mathematics and logic, rather more than in other scientific disciplines (although experiments that didn't

give the expected result have frequently led to key discoveries in science). The rationale behind the search for counterexamples is based on the notion that it can often be as valuable to know what is not universally true as to know what is. Furthermore, falsehood can be established far more easily than truth.

3.3 The use of vignettes

The examples given have come about as a result of considering some of the logical consequences of the notions surrounding the Heinrich triangle. This has been very much influenced by the presence in the project team of a mathematician. This leads to a presentational difficulty since the undue use of technical mathematical terminology would not help to clarify issues for a general healthcare audience. Instead, we have adopted a format whereby mathematical details are for the most part well hidden and their consequences are illustrated by describing a number of hypothetical yet credible vignettes. These give pen portraits of sets of circumstances in which credence in the Heinrich triangle could lead to illogical or unfounded inference or unexpected and perhaps counterintuitive analysis results. The use of the term "Cautionary Tales" has been used to describe this collection of vignettes since hopefully most have a "moral" in that they indicate a lesson that may be learnt.

3.4 Vignettes related to the use of Heinrich's triangle

It should be said that the initial reaction of the mathematical member of the research team (SG) to the notion of a fixed relative frequency of different forms of safety incident was extremely sceptical. From a systems viewpoint, safety incidents often occur as the result of complex interactions and the chance concatenation of different events and circumstances. To a mathematician, the notion that there is a fixed homeostatic mechanism at work that maintains the same relative frequency of different categories of incident seems bizarre.

In view of this, several vignettes have been constructed to illustrate circumstances where such behaviour would not be expected or, even if it were, this would not help the monitoring process. However, in the interests of equity, it is perhaps worth starting with a vignette where the homeostatic principles of Heinrich triangle might be expected to occur.

3.4.1 Vignette 1 - a system exhibiting homeostasis

A wayward G.P. habitually forgets to check whether his patients have a penicillin allergy before prescribing it. Each time this is done is certainly an error event. However, for most patients no harm is suffered since they are not in fact allergic. But some patients have a mild allergy and undergo a mild reaction; and some unfortunate patients suffer a major reaction.

Concerned colleagues convince him to change his ways, so that instead of forgetting to check allergy status on 80% of occasions, the negligence rate is reduced to 40%. As a result, the frequency of both mild and major reactions is halved.

<div style="border:1px solid black; padding:10px;">

Moral

There are circumstances where homeostasis in the relative frequency of different categories of outcome is to be expected.

</div>

3.4.2 Vignette 2 – a system with no homeostasis

A version of Russian roulette is played with a revolver that has six chambers. One is loaded with a live cartridge, two are loaded with blank cartridges and the other three are left empty. The chambers are spun several times, the player places the gun against his head and pulls the trigger.

Analysis of outcomes from this dangerous game shows a remarkably consistent pattern. The relative frequencies of deaths, minor injuries (powder burns) and no injuries were in the ratio 1:2:3.

In an effort to make the game safer, Heinrich's principle was followed and attention was cast on the minor injuries to see if remedial action could be taken. A new loading pattern was adopted with one live cartridge, one blank and four chambers left empty. This was tremendously successful and halved the proportion of powder burn injuries. However, there was no effect on the proportion of deaths, in contravention of Heinrich's concept.

> **Moral**
>
> The existence of a fixed ratio between the relative frequency of different events does not necessarily mean that this ratio will be preserved if the system is altered to change the absolute frequency of a subset of the events.

3.4.3 Vignette 3 – a system exhibiting risk migration whereby it is effective to promote minor outcomes.

A new version of Russian roulette was developed. Here a box of live cartridges and two boxes of blank cartridges are thoroughly mixed in a sack. Then the revolver is loaded with three cartridges drawn at random. The player then places the revolver against his head and pulls the trigger.

Again analysis of outcomes shows a remarkably consistent pattern and the long term outcomes of deaths, minor injuries and no injuries are in the ratio 1:2:3.

The game evolves and it is decided to mix one box of live cartridges with 5 boxes of blank cartridges before choosing three at random from the mix to load into the revolver. The effect of this was to increase the proportion of powder burn injuries, but it was also found that the proportion of deaths halved.

> **Moral**
>
> There may be circumstances whereby promoting the occurrence of minor adverse events can reduce the frequency of major adverse events.

3.4.4 Vignette 4 – a statistical problem associated with extrapolation

Suppose a study has been carried out of accidents within a hospital that occurred when transferring patients from one ward to another whereby a patient falls from a trolley. Suppose the study found that such accidents are relatively rare and that the proportion of injury accidents that result in death is 8.3% (these are fictitious data broadly comparable to proportion of serious road traffic injuries that result in death).
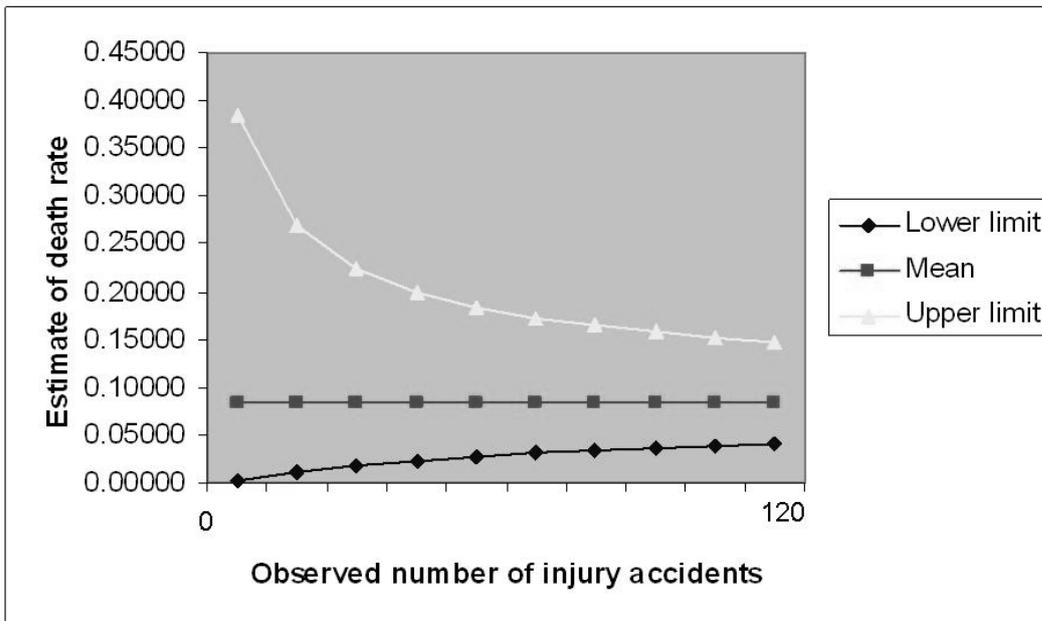
Figure 4: Upper and lower 95% confidence intervals for estimate of proportion of serious injury accidents that result in death, given that what is observed corresponds to a rate of 8.3%.

Figure 4 shows how broad the confidence intervals are for the underlying death rate dependent on the number of cases observed, given that the proportion of deaths observed is 8.3%. Small amounts of data on harm are extremely ineffectual in indicating the true proportion. For example, ten cases may indicate a death rate anywhere between 1% and 26%. Falls from trolleys during transit are presumably very rare so an inordinate number of observations would be required even to accumulate outcome data on, say 100 such accidents. Even with such a sample size, the upper estimation limit in this example is roughly twice the size of the death rate estimated. Extrapolation from a single study with such wide margins of error is clearly problematic. So, for example, estimating the number of deaths that would be avoided by introducing a national programme aimed at reducing trolley accidents would give very imprecise estimates that are possibly not meaningful.

Moral

In cases where the type of accident being studied is rare and where the adverse outcome rate is small, confidence intervals for what that rate is are so broad as to make extrapolation very imprecise. It is hard to test statistically whether an intervention truly has an effect.

3.4.5 Vignette 5 – the central role of rules for categorising events

Some outcomes do not neatly fit into three categories. Consider the example of birth weight of singleton babies, which over the population as a whole is approximately normally distributed, having the well known bell shaped distribution as shown in Figure 5. The question arises how a continuous measure such as birth weight can be used to categorise babies as "normal", "underweight" or "grossly underweight".
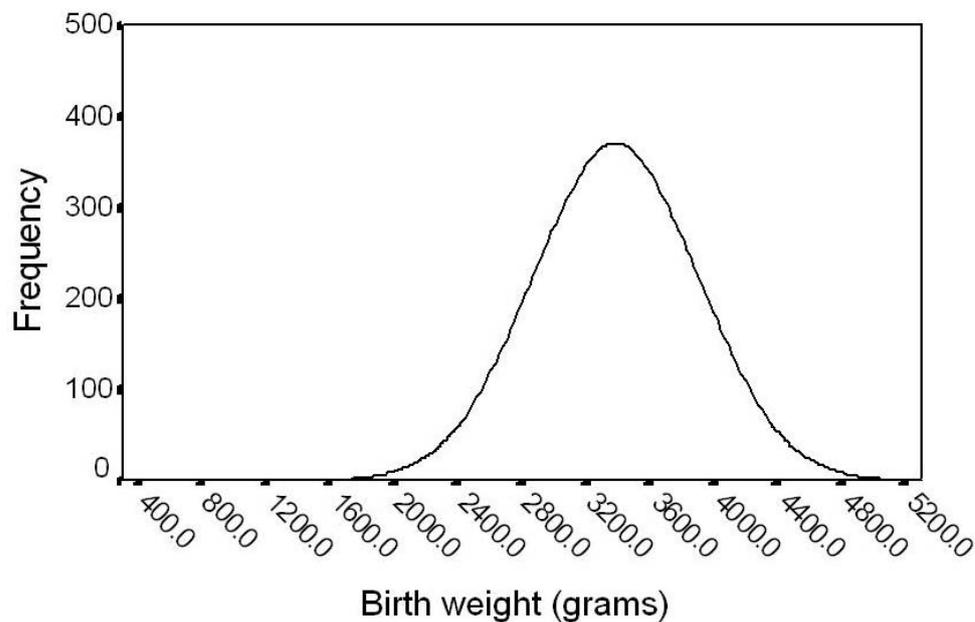
Figure 5: A normal distribution fitted to the birth weight of babies resulting from singleton pregnancies.

An apparently reasonable procedure is to use two category boundary values v_1 and v_2 to determine the assignment; thus a baby weighing more than v_2 would be categorised as 'normal', one weighing between v_1 and v_2 would be categorised as "underweight" and one below v_1 as "grossly underweight".

In the context of the Heinrich concept, it is natural to examine what relative ratios one would expect for given values of v_1 and v_2 assuming an underlying normal distribution.
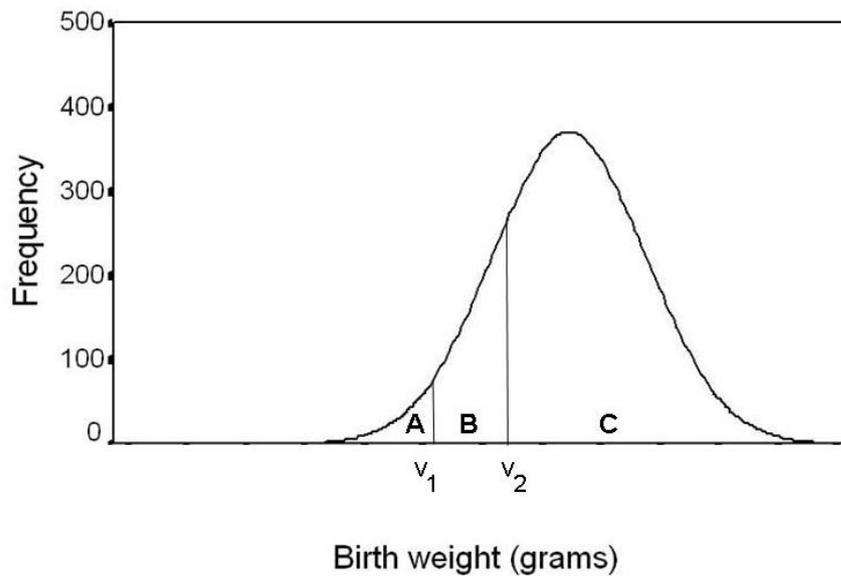
Figure 6: Illustrating the use of category boundaries v1 and v2 to determine which babies are deemed 'normal', 'underweight' or 'grossly underweight'

Omitting the mathematics, the relative ratios correspond to the areas under the curve in the three regions A, B and C of the normal distribution shown in Figure . It is common practice in medical research to choose category boundaries using normal distributions in this way. Thus v_2 may be chosen so that region C has an area 95% of the whole while v_1 is chosen so that region A has an area 1% of the whole. Thus the Heinrich ratio would be 95:4:1.

Yet the actual values of v_1 and v_2 are arbitrary and could just as well to be chosen to divide the population of neonates into three other categories and indeed it is also common to use a 90% cut-off rather than 95% to correspond to "abnormality", which would give a different Heinrich ratio, for example 90:7:3 or 90:6:4 would both have some rationale.

A pure mathematician musing on this turned the question on its head and posed the following problem: Given the freedom to choose v_1 and v_2, what Heinrich ratios can be achieved?

Perhaps surprising to non-mathematicians, the answer is that any relative ratio can be achieved, so long as the three components of the ratio are positive numbers (however small). Further, this does not depend on the underlying probability distribution being

normal. It is sufficient that the probability distribution is continuous and that the set of values for which the probability is non-zero is contiguous. For completeness, a formal mathematical proof of this is given in Appendix 1.

Moral

In cases where there is no natural three way categorisation of events as major, minor and no-harm, then the way chosen to categorise events can have a major impact on the resulting Heinrich ratio and in principle any ratio can result.

Here we would like to draw the attention of the reader to our extensive review of medication error literature (Appendix 3). We comment in detail the many methodological limitations of medication error research including the lack of agreement concerning how to define basic terms such as medication error and the lack of valid and reliable methods to assess (potential) patient outcome of medication errors. This review shows that there is certainly no natural three way categorisation for medication errors.

3.5 Summary

In this Chapter we have shown that

1. A Heinrich ratio may occur in certain circumstances, so that a simple intervention may lead to a proportionate reduction in errors of all categories of harm.
2. Even if there is a Heinrich ratio, some interventions may just affect two categories, rather than all three proportionately
3. If harmful incidents are rare events, estimations of the rate of harmful events from data are very imprecise.
4. The Heinrich ratio will be extremely sensitive to the definitions used to categorise the data

In the next Chapter we describe a method of visually displaying the Heinrich ratio.

4 A graphical method for displaying safety data classified into three categories

4.1 Introduction

In this Chapter, a graphical method for displaying safety data is described. From a statistical viewpoint, the methods are not new and are based on the use of what are known as barycentric coordinates. The use of such methods in relation to safety research seems novel. Furthermore, confidence regions will be constructed to allow statistical comparisons of different ratios. We require this method to be able to investigate the Heinrich ratio using empirical data.

The method is illustrated using data from a study concerning outcomes from emergency department visits in the United States,[21] this having the advantage of being medical data with fairly clear definitions.

4.2 Developing a visual representation of the Heinrich ratio

Suppose that a given study reports x no harm incident, y minor incidents and z major incidents, then the Heinrich ratio is $\dfrac{x}{x+y+z} : \dfrac{y}{x+y+z} : \dfrac{z}{x+y+z}.$

It would be convenient to compare different studies using a scatter plot, but on the face of it this seems complicated since the scatter plot involves three coordinates and thus the scatter is in three dimensional space, which in general is difficult to visualise.

However, given that x, y and z are always non-negative, and the relative ratios always sum to 1, then the point with coordinates $(\dfrac{x}{x+y+z}, \dfrac{y}{x+y+z}, \dfrac{z}{x+y+z})$ always lies somewhere in the triangle bounded by vertices where the plane with equation $x+y+z = 1$ meets the x, y and z axes. This is an equilateral triangle T as shown in Figure .
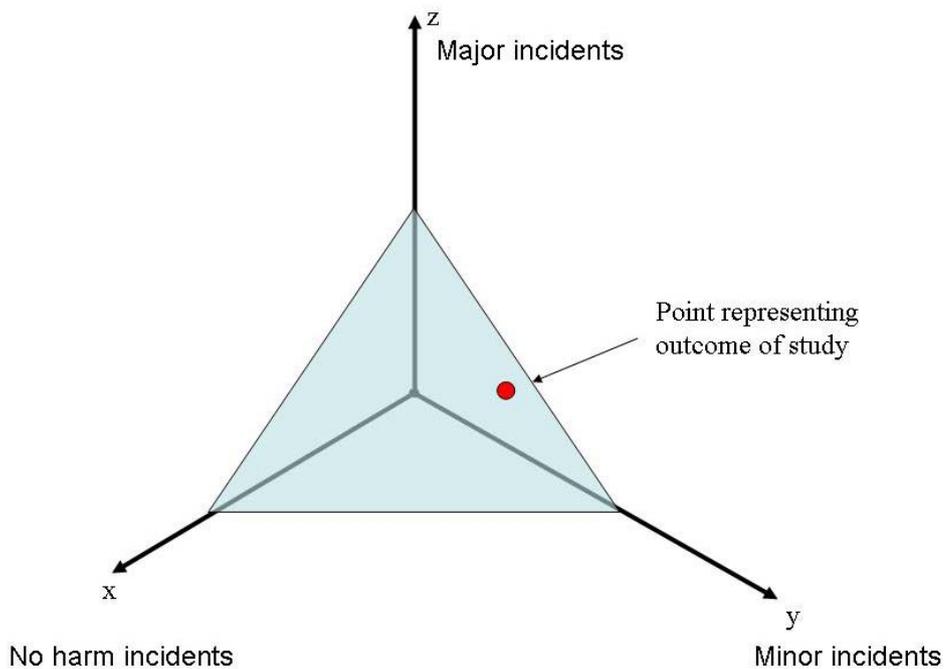
Figure 7: Displaying three relative frequencies as a point within an equilateral triangle T in three dimensional space.

In visualising Figure , it might help to imagine a room, the *x* and *y* axes being the lines corresponding to where the floor meets two walls, and the *z* axis being the line where the two walls meet. The equilateral triangle T can then be thought of as a triangular glass plate manoeuvred so that it rests against both walls.

Thus, for a given study, it is possible to plot a point in the triangle T that represents the three relative ratios. In addition, it is technically feasible to plot an approximately elliptical region around the point representing the 95% confidence region, (generalising the notion of the 95% confidence interval). Technically, this is rather challenging, however the region can be approximated by a hexagon which is computationally rather easier to plot.

A certain amount of mathematics is needed in order to convert this three-dimensional picture into terms that can be plotted onto paper (or a two-dimensional computer screen). Details of this are given in Appendix 2 which also discusses the construction of the confidence intervals.

4.3 Illustration of the method in the case of A&E outcomes

It is useful to illustrate the notion of a triangle plot, although for this purpose we have chosen not to use safety data here, but use data from a study of accident and emergency visits from the US [21] (we already referred to this study in section 0). Table 6 shows the data. These data are summarised graphically by the triangle plot shown in Figure . Data from medication error research will be analysed with this method in Chapter 5.

	Death	Hospitalisation	Emergency department visit
Self inflicted gunshot wound	1721	191	198
Assault related gunshot wound	1002	1090	1609
Self inflicted poisoning	508	8540	9847
Assault related struck	24	2076	52111
Assault related cut/pierced	193	977	5292
Self inflicted cut/pierced	29	427	2203

Table 6: Classification of the outcome of patients visiting the emergency departments. Data taken from Wadman et al. [21]
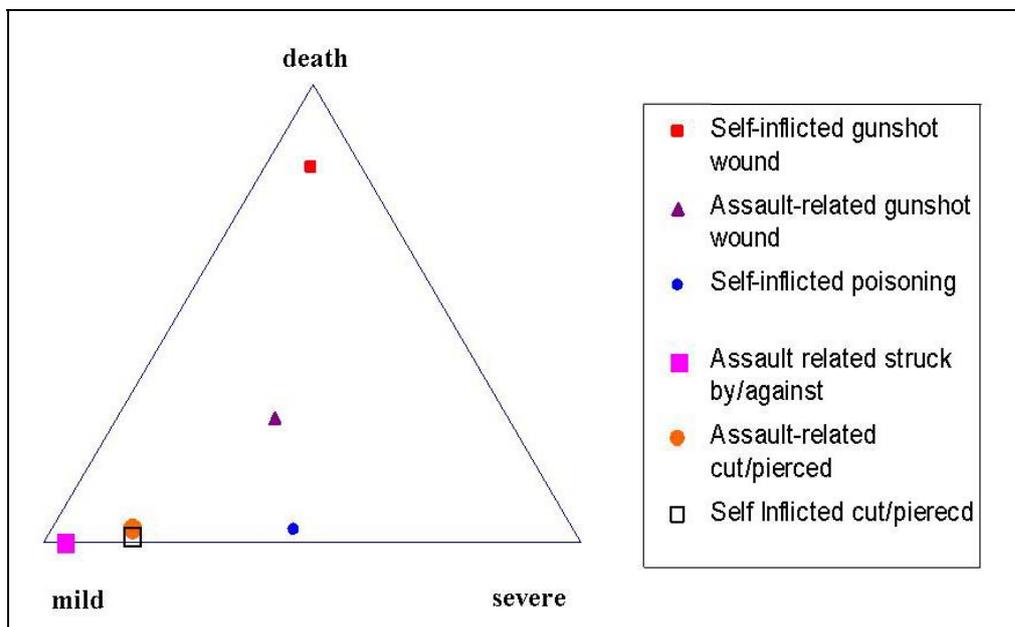
Figure 8: A triangle plot of outcome data from emergency departments subdivided according to the nature of the admission. (The category 'mild' refers to emergency department visits and 'severe' refers to hospitalisation).

At a glance, this figure shows the considerable variation that exists in outcome according to the type of case involved. Perhaps unsurprisingly, a much higher relative

proportion of cases of gunshot wounds, particularly those self-inflicted, result in death than the relative proportion of deaths resulting from self inflicted poisoning, although roughly half these cases result in hospitalisation.

4.4 Discussion

This graphical method for displaying data is not new and relies on the use of what are technically known as "barycentric coordinates". However, the use of this method in relation to safety data appears to be novel.

Such triangle plots give a succinct and immediately comprehensible method for interpreting complex data classified into three categories. Furthermore, the method constructing confidence regions can be used for identifying if ratios are statistically different. In the next Chapter we use this approach to compare data from the literature and establish whether there is a unique Heinrich ratio for medication errors, or whether different studies produce significantly different results.

5 An analysis of medication error data using the new graphical method

5.1 Background

In Chapter 4 we presented a new graphical method for displaying safety data classified in three categories of (potential) harm. In this Chapter we use this method to display data from medication error studies to explore whether there is a Heinrich ratio for medication errors.

5.2 Data sources

We undertook a literature search to identify eligible studies.

Inclusion criteria:

Original studies which reported results of the incidence of medication errors in the hospital setting by actual or potential outcome in at least three categories. Studies had to provide sufficient detail of their methodology including data collection methods and data analysis to judge the quality of the study. In particular studies had to report the definition of the medication error, the exact method of data collection, a description of how the medication error rate was calculated, and a description of how the severity of the medication errors were determined.

Exclusion criteria:

Studies were excluded if the results of the study were not reported according to severity equivalent to Heinrich's three categories (or if the results could not be recategorised). Data were categorised in the following three categories:

1. MINOR: harmless/minor/no injury errors
2. MODERATE: errors with moderate severity
3. SEVERE: serious/severe/fatal errors

Studies were also excluded if their results were based on spontaneous error reporting systems as, because of known underreporting, and because there is an unknown bias in spontaneous error reporting, i.e. it is unknown whether severe errors are reported to the same extent as no harm errors (see also Appendix 3 for a more detailed discussion of the different data collection methods)

Eleven studies were included. Details of these studies are summarised in (Table 7).

Reference	Minor	Moderate	Severe	Country, clinical area	Data collection methods	Assessment method for severity of errors
Adverse drug events and medication errors (all types)						
Bates et al., 1995 [28]	525	4	1	USA general medicine and intensive care	self reports, review of medical charts and medication orders	consensus of two physicians
Kaushal et al., 2001 [29]	611	5	0	USA, paediatrics	self reports, review of medical charts and medication orders	consensus of two physicians
Prescribing errors						
Dean et al., 2002 [30]	160	224	142	UK, teaching hospital	review of medication orders	consensus of pharmacist and physician
Dean et al., 2002 (unpublished data)	160	289	123	UK, teaching hospital	review of medication orders	consensus of pharmacist and physician
Lesar, 1997 [31]	537	96	43		review of medication orders	one or more health professionals
Administration errors						
Dean and Barber, 2000 [32]	199	58	0	UK general medicine, surgical ward	observation of drug administration	mean score of four health professionals (pharmacist, physician, nurse) [33]
Taxis and Barber, 2004 [34]	22	39	4	Germany, surgical ward, intensive care	observation of drug administration	mean score of one pharmacist, one nurse, one physician [35]
Taxis and Barber, 2003 [25]	102	144	3	UK, different specialities	observation of drug administration	mean of four health professionals (pharmacist, physician, nurse) [33]
van den Bemt et al., 2002 [36]	81	50	0	Netherlands, intensive care	observation of drug administration	consensus of two pharmacists
Hartley and Dhillon, 1998 [37]	198	44	12	UK, general medicine, surgical wards	observation of drug administration	consensus of three pharmacists

| Tissot et al., 1999 [38] | 51 | 55 | 26 | France, intensive care | observation of drug administration | classified by one physician |

Table 7: The incidence of different types of medication errors reported from 12 studies

5.3 Graphical comparison of studies

A triangle plot of the data summarised in Table 7 is shown in Figure.
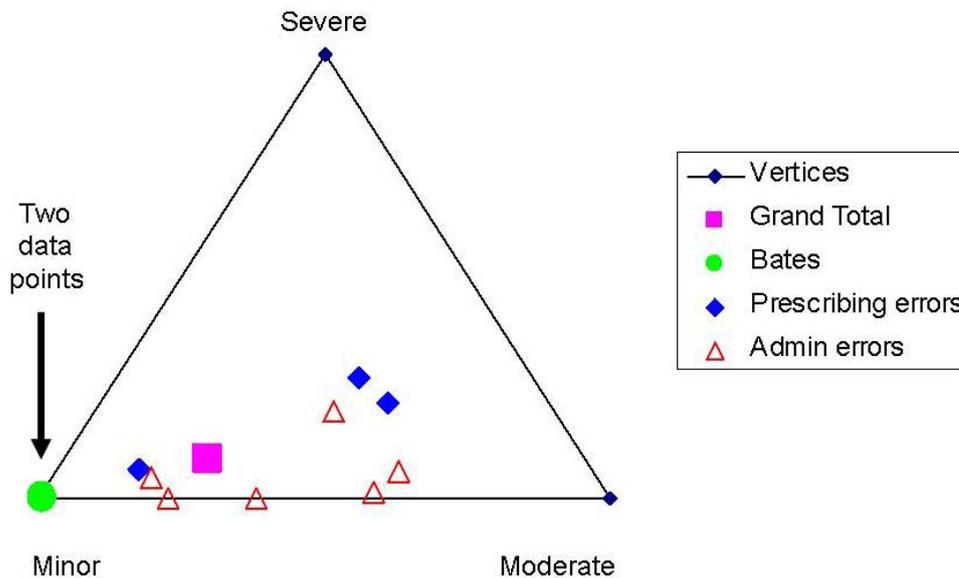
Figure 9: A triangle plot illustrating the relative frequency of different forms of medication error based on data from Table 7

This plot exhibits considerable scatter, lending little support for the Heinrich triangle concept that there should be a relatively fixed relationship between the relative frequencies of mild, moderate and severe medication errors. Although there is a "grand total" figure, which reflects the relative frequencies of all the data combined (shown by the square symbol), this clearly does not reflect the overall data which have a high degree of inherent variability. This is a central issue in this report, and so we now compare this total with each individual study, showing the 95% confidence regions.

In each case the confidence regions do not remotely overlap – lending support to the view that there is a systematic and statistically significant disparity between the 'grand total' relative ratio and each of the constituent data sets.

In the section describing triangle plots, it was shown that these 95% confidence regions are elliptical and can be closely approximated by a hexagon, which is computationally more convenient to display (Appendix 2). When such a confidence region is displayed for the "grand total" shown above in Figure, the overall sample size is sufficiently large that the confidence region is very small, comparable in size

to the symbol used to display the single data point. This is convenient since in the following series of triangle charts, only one confidence region needs to be displayed – that for the data from the study being examined. In some other cases, such as the ones displayed in Figure and Figure , the 95% confidence regions from the individual studies are also so small they can not be distinguished from the point.
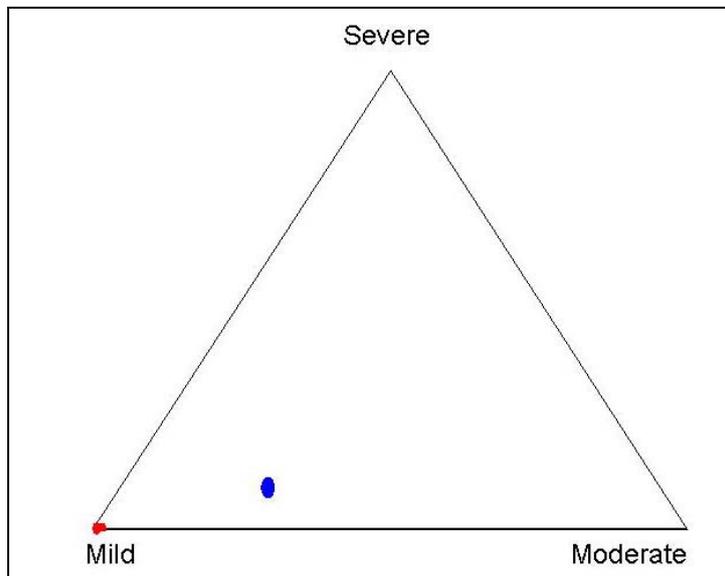
Figure 10: Triangle plot comparing the grand total relative ratios with data taken from Bates et al., 1995 [28] (study on adverse drug events and all types of medication errors) (point is almost inseparable from the left vertex)
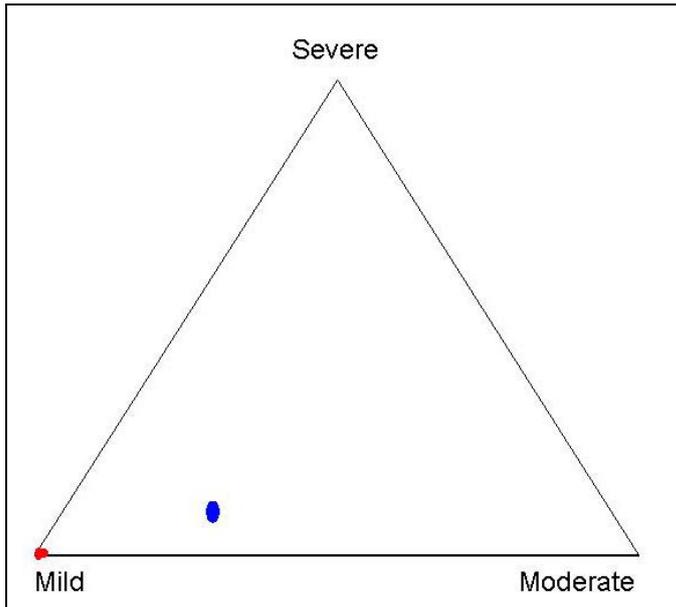
Figure 11: Triangle plot comparing the grand total relative ratios with data taken from Kaushal et al., 2001 [29] (study on adverse drug events and all types of medication errors) (point is almost inseparable from the left vertex)
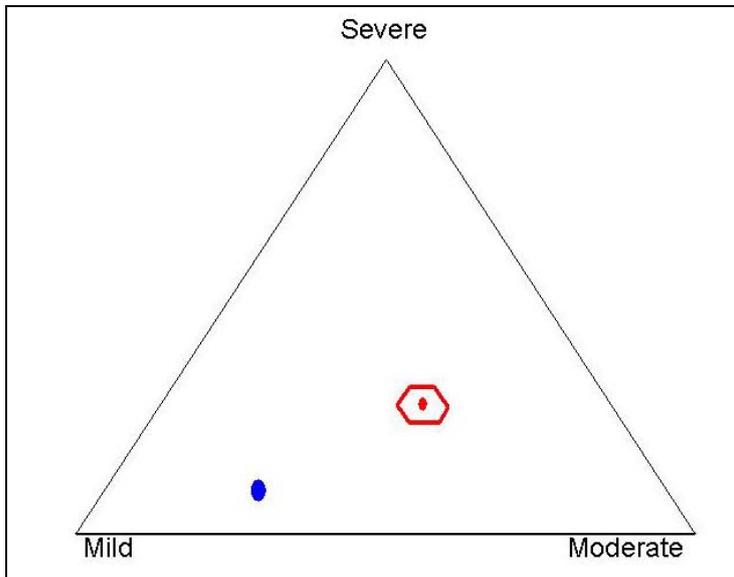
Figure 12: Triangle plot comparing the grand total relative ratios with data taken from Dean et al., 2002 [30] (study on prescribing errors)
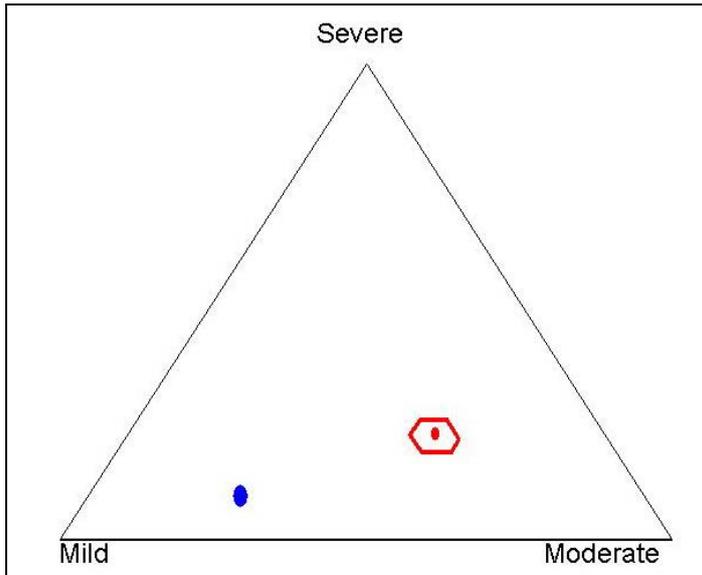
Figure 13: Triangle plot comparing the grand total relative ratios with data taken from Dean et al., 2002 (unpublished data) (study on prescribing errors)
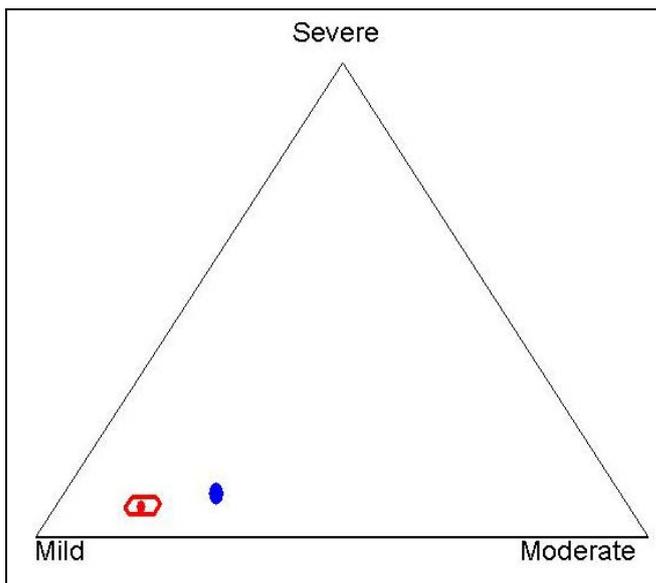
Figure 14: Triangle plot comparing the grand total relative ratios with data taken from Lesar, 1997 [31] (study on prescribing errors)
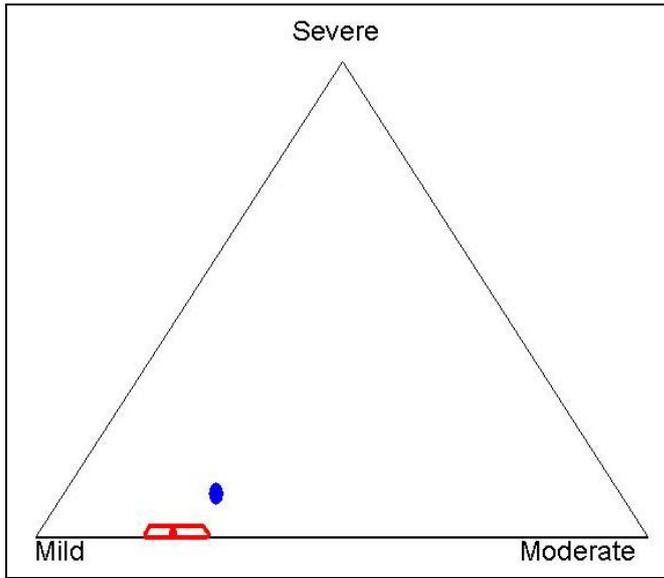
Figure 15: Triangle plot comparing the grand total relative ratios with data taken from Dean and Barber, 2000 [32] (study on administration errors)
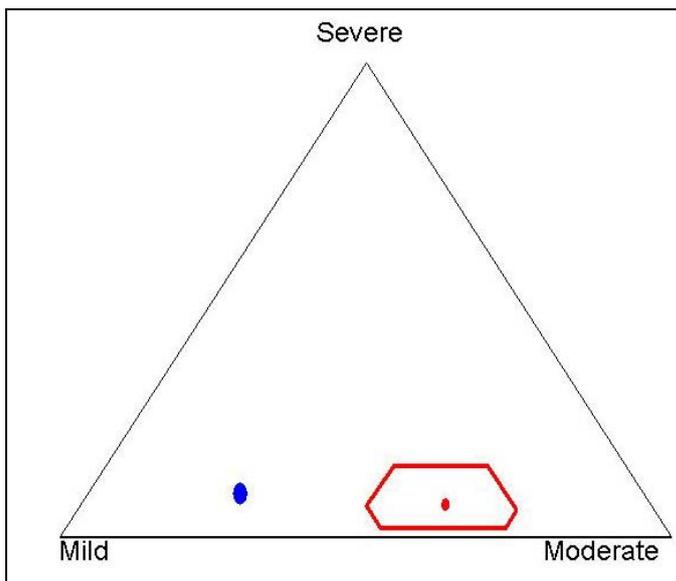
Figure 16:Triangle plot comparing the grand total relative ratios with data taken from Taxis and Barber, 2004 [34] (study on administration errors of intravenous medication)

43
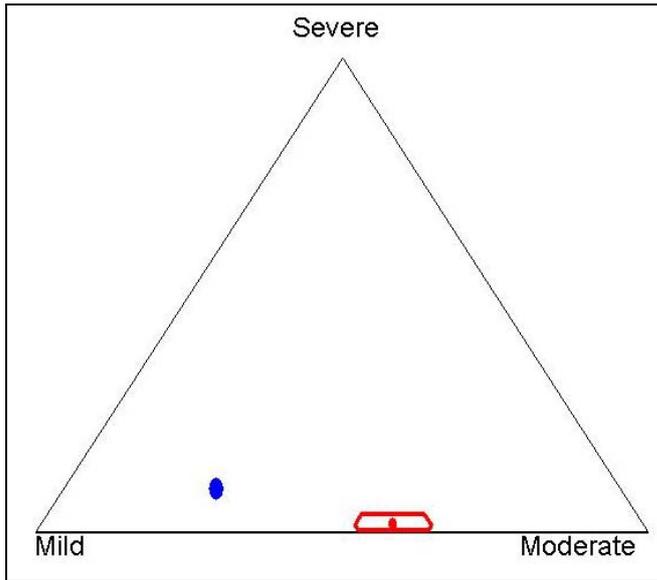
Figure 17: Triangle plot comparing the grand total relative ratios with data taken from Taxis and Barber, 2003 [25] (study on administration errors of intravenous medication)
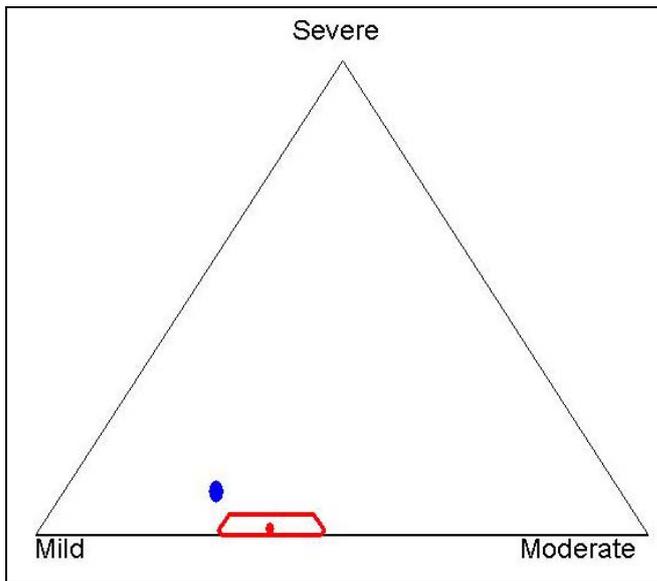
Figure 18: Triangle plot comparing the grand total relative ratios with data taken from van der Bemt et al., 2002 [36] (study on administration errors of all routes of administration)
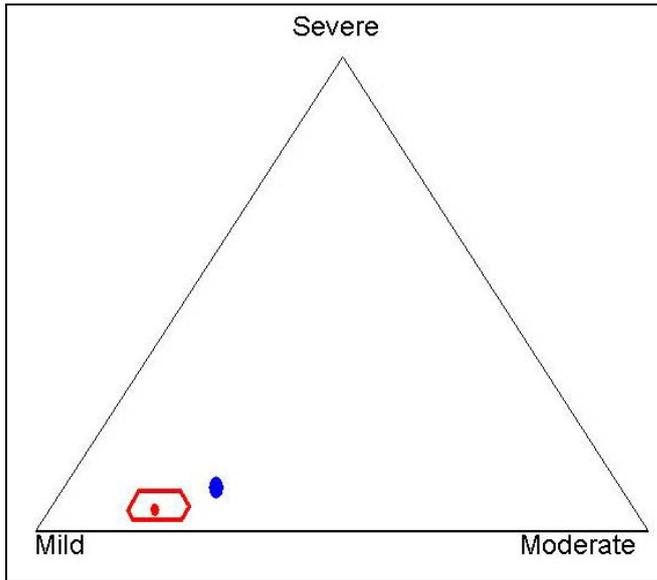
Figure 19: Triangle plot comparing the grand total relative ratios with data taken from Hartley and Dhillon, 1998 [37] (study on administration errors of intravenous medication)
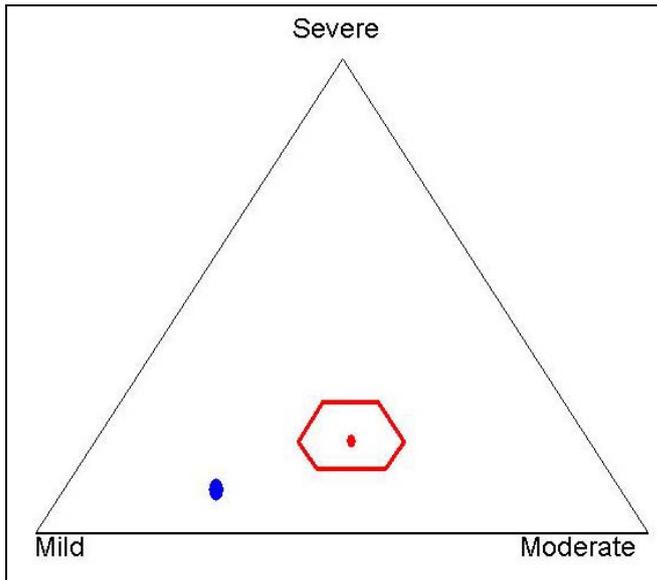
Figure 20: Triangle plot comparing the grand total relative ratios with data taken from Tissot et al., 1999 [38] (study on administration errors of all routes of administration)

5.4 Discussion

We find considerably variability between studies concerning the relative proportions of minor, moderate and severe medication errors, and the "grand total" is substantially and significantly different from all the relative proportions of the constituent studies. Some of the variability may be explained firstly by systematic differences in medication error rates by setting or stage of the process, and secondly

by differences due to variability in data collection and classification methods. We discuss both of these issues in more detail below. Nevertheless, our findings do not support the notion of a stable Heinrich ratio for medication errors.

Does the Heinrich ratio depend on setting or type of error being studied?
We included studies from a range of different countries, settings and clinical areas as outlined in Table 7. Some of the studies focused on errors occurring in specific stages of the medicines use process such as prescribing or administration errors, others included preventable adverse drug events related to all steps in the process. All of these may systematically influence the medication error rate. For example, it has been suggested that paediatric patients have a higher risk of experiencing medication errors than adult patients.[39] Similarly, it has been suggested that most serious errors result from prescribing errors rather than administration errors.[40] Therefore we would expect different "Heinrich ratios" in different settings or for different stages of the process. However, we do not find an obvious trend of clustering of studies which identified errors in similar settings, for example the studies carried out in intensive care.[36;38] Similarly, there does not seem to be an obvious trend for prescribing error studies or administration error studies, although some of the variability may be due to variability between hospitals.

Does the Heinrich ratio depend on study methodology?
We present a substantial review of medication error research methodology in Appendix 3. We show in detail the many methodological limitations including the lack of standardisation in:
- defining medication errors
- data collection methods
- methods to analyse the severity/outcome of the medication error

These methodological limitations may partly explain the great variability in Heinrich ratios found in this chapter. Different definitions for medication errors were used. For example the study by Dean et al. [30] used a consensus based definition of a prescribing error whereas some other studies based their definition on implicit judgement of pharmacists.[31] Such differences in definition may mean that some studies collect more harmless medication errors in relation to harmful medication errors than others.

Type of data collection method may also influence the resulting ratio. Interestingly, we find both studies which were based on actual outcome (i.e. collecting data on preventable adverse drug events) [28;29] in the left corner of the triangle, i.e. these studies found a relatively small proportion of severe and moderate errors in relation to minor errors. All other studies were process based studies which collected data on medication errors and used different methods to predict their potential outcome. This method in general does not take into account the frequency with which such errors result in true adverse outcomes and therefore may overestimate the proportion of severe and moderate medication errors.

Finally, many different methods are used to determine outcome of medication errors and different categories are used to report the results thereof. Furthermore, we had to reclassify the errors to fit into major – moderate – minor categories for studies using more than three categories. Table 8 shows a few examples of how we classified data. For example, for the study by Bates et al. [28] we decided to classify all "potential adverse drug events" as minor events as they did not result in actual harm to the patient. Studies such as Tissot et al. [38] reported their results in four categories, so we classified potential fatal and life threatening errors as major errors. We took great care in this process to be as consistent as possible across studies. However, some variability remains when authors chose different cut off points to distinguish between the different levels of harm. For example, the category of minor errors were defined as having "no risk for patients and no implications"[37], as "very unlikely to have an adverse effect on the patient"[33] or as "potentially significant".[31] These definitions suggest that there may have been slightly different cut off points to differentiate between potentially minor and moderate errors. As we have already highlighted in Chapter 3 (Vignette 5), the cut off point between the categories greatly influences the ratio.

Classification for Heinrich ratio	Bates et al [28]	Lesar [31]	Tissot [38]
Major	Life threatening preventable adverse drug events	Potential fatal/severe	Potential fatal and potential life threatening
Moderate	Serious preventable adverse drug events	Potential serious	Potential significant
Minor/no-injury errors	Life threatening/serious/significant potential adverse drug events (including intercepted events) plus medication errors	Potential significant	Minor

Table 8: Examples of reclassifications to establish Heinrich ratios for individual studies

Is there a Heinrich ratio in a narrow well defined research setting?

Based on the analysis of the data we find that there is little evidence for a stable Heinrich ratio for medication errors. There is some indication that if one research group, using the same methods, definitions, studying the same type of medication error in the same setting over time might observe a stable Heinrich ratio. This could indicate that a fairly safe set of errors was studied, because it involved a low risk process (e.g., medication errors associated with oral drug administration in hospital). However, finding a stable Heinrich ratio in just a very narrow research setting does not provide the robustness required by the NPSA. Nor does a stable Heinrich ratio mean that any changes in minor incidents would predict a proportional reduction in harm.

5.5 Conclusion

There is considerably variability between studies concerning the relative proportions of minor, moderate and severe medication errors. Combining data from all the studies available gives a "grand total" that can be used to derive relative proportions. However, this grand total figure is not representative; it is substantially and significantly different from all the relative proportions derived in each of the constituent studies.

In this Chapter we have investigated the Heinrich triangle using data from medication error research, finding little support for the concept. This complements our findings investigating the logical and mathematical basis of the Heinrich triangle in the previous Chapters. At this point, the reader may go straight to the final Chapter where we summarise the main conclusions from our report.

However, the authors were also interested in investigating the Heinrich triangle using empirical data from a different context. As we have highlighted repeatedly, one of the limitations in using medication error data for the Heinrich triangle has been the lack of standardisation within these data. One of the cautionary tales in Chapter 3 highlighted the sensitivity of the ratio to the position of the boundaries between categories. Perhaps our failure to establish a stable ratio just reflected different definitions and methods? Therefore we were interested in testing the Heinrich triangle using another set of data of "higher quality". Data from road traffic accidents seemed suitable because of the good quality of the data and because outcomes are also reported in three distinct categories. The following chapter explores whether we find support for the Heinrich triangle in road traffic accident data.

6 Road traffic accidents under the microscope

6.1 Illustrating the use of the triangular plot using road accident data

The data used in this Chapter concern the outcomes of road traffic accidents in Great Britain recorded on an annual basis between 1993 and 2003.[41] In the field of road traffic safety, meticulous records are kept of every road traffic injury accident that is reported to the police. Outcomes are classified as deaths, major injury (requiring hospital admission) and minor injury. Great pains are taken to ensure that data are complete and a standardised data collection form is used which provides little scope for non-uniformity in what is recorded in different centres. In spite of all this effort the Department of Transport suggests that there is still some under-reporting, under-recording and misclassification leading to underestimating the number of seriously injured casualties; however, for the purpose of our project these are assumed to be constant over time and therefore do not affect the validity of our conclusions.[41]

6.2 Overall trends in road traffic accidents in Great Britain between 1993 and 2003

The achievements in improving road safety have been remarkable and during the period concerned there was a marked decline in both fatalities and serious injuries, in spite of increasing car ownership and total travel and variations in the annual total numbers of road traffic accidents. These overall trends are shown in Figure 21 and Figure .
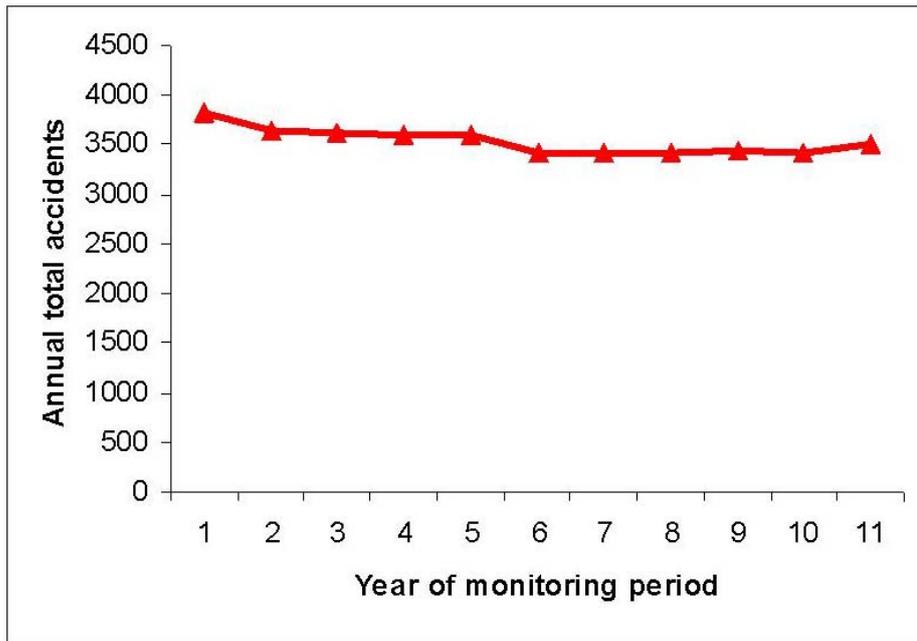
Figure 21: Annual numbers of fatal road traffic accidents for Great Britain during the period 1993 - 2003
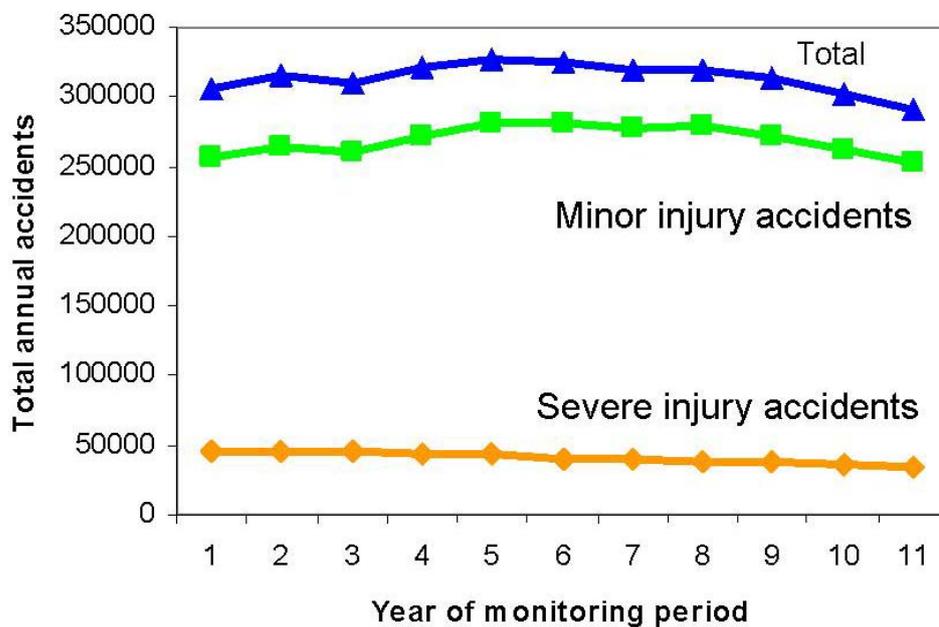
Figure 22: Annual numbers of all, of minor injury and serious injury road traffic accidents for Great Britain during the period 1993 - 2003

6.3 Using triangle plots to examine road traffic accident data

These systematic variations in the overall numbers of different types of accident suggested that this topic would be a useful means for investigating Heinrich's concept that the relative proportions of the three accident types should be constant. Also, road traffic safety is a field for which considerable amounts of data are already available, conveniently classified into three severity groupings, with uniformity of the criteria used to classify cases, it also gives a useful additional example of the use of triangle plots for displaying complex safety data.

The triangle plot shown in Figure shows the annual relative ratios of the three categories of road traffic accident outcomes. On the face of it, there appears to be remarkable consistency between the 11 years, so much so, that it is difficult to plot the individual points to distinguish one from the others.

Originally, this remarkable stability from one year to the next was taken to indicate some degree of homeostasis suggesting that there might indeed be some substance to Heinrich's concept. However, there is potentially a "floor" effect at play; since the proportion of death accidents is relatively small and cannot fall below zero, thus inevitably this might induce bunching.
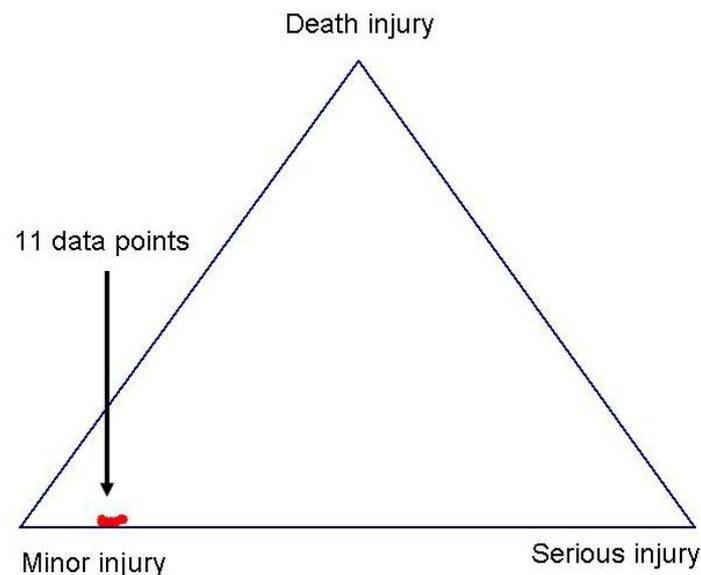
Figure 23: A triangular plot of the annual relative frequency of outcomes for road traffic accidents in Great Britain between 1993 and 2003.

To examine this further, the data were examined in closer detail using the graphical methods illustrated in Figure .
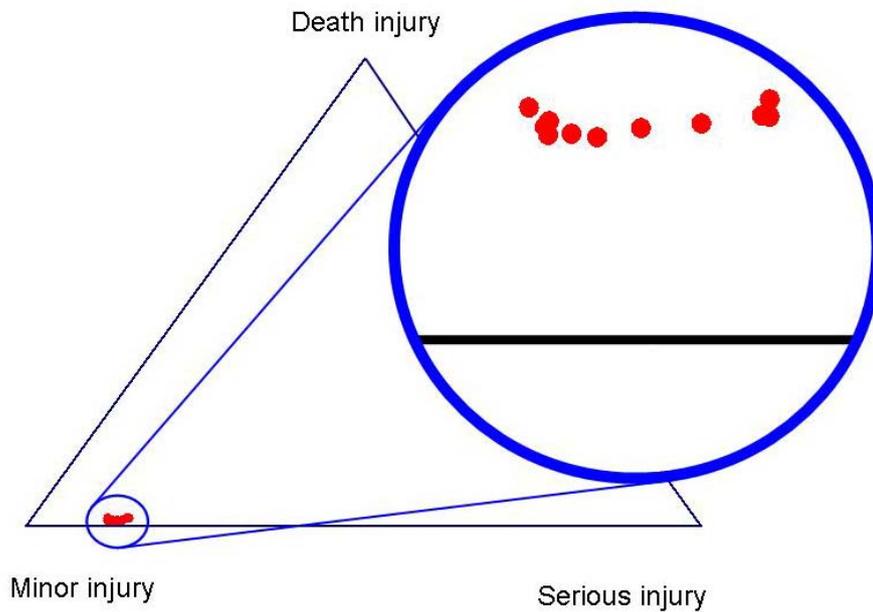
Figure 24: Examining the triangle plots of annual relative ratios of road accident type in closer detail.

This closer examination reveals that the cluster of points is very much parallel to the base of the triangle, indicating that the relative proportion of accidents involving a death has remained approximately constant during the 11 year period 1993 to 2003. On the other hand there is much more variability concerning the split between minor and serious injuries.

Intrigued by the regular nature of the cluster of data points, an even more detailed examination of the graphical nature of the data was undertaken, shown in Figure .
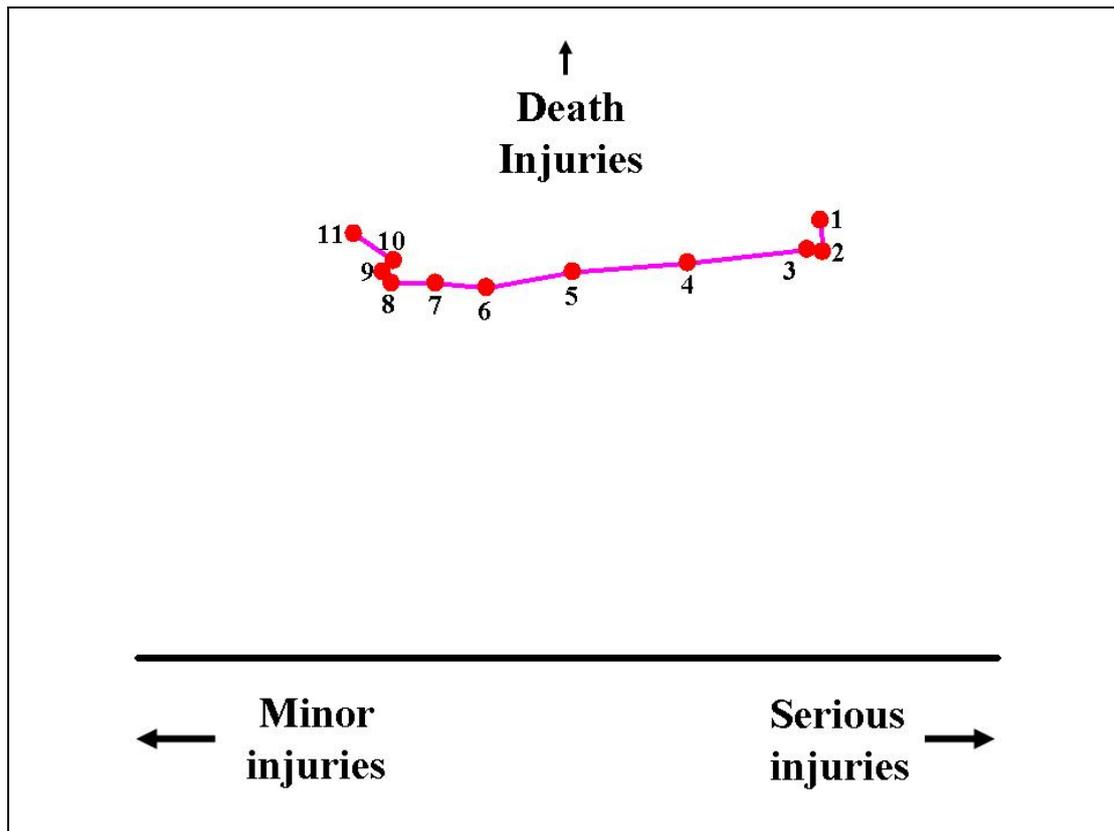
Figure 25: Triangle plots of annual relative ratios of road accident type labelled according to the year of the monitoring period (1993 – 2003). Successive data points have been joined by a line (1993=1 to 2003=11)

6.4 Road traffic accidents and Heinrich's concept

In Figure , to aid interpretation, successive data points have been joined by a line, although for two clusters (years 2 and 3, and years 8, 9 and 10) the data points are so close that they obscure these lines.

The data set is clearly very structured, so much so that the notion of using formal statistical methods to establish this is possibly facile. During the course of the period 1993 to 2003, the proportion of all road accidents that involved a death remained approximately constant. At the same time, there was a systematic reduction in the relative proportion of accidents that result in serious injury compared to minor accidents. This is consistent with much of the activity that underlies the promotion of road traffic safety: improved structural safety of vehicles, traffic calming in urban areas and drink driving policies. Part of the thinking underlying these measures is both to reduce the overall accident rate and, for those accidents that occur, increase the chances that the results are minor injuries at most.

However, the systematic dynamics of the changing pattern of road traffic accident outcomes conflicts with what would be expected from the Heinrich triangle, that the relative proportion of the three categories of accident should be constant. This is clearly incompatible with the evidence shown in Figure which shows that beyond reasonable doubt it changes systematically.

As shown in Figure , year on year, there has been marked trend for the total number of serious injury accidents to decrease. Under the terms of Heinrich's concept, this should be reflected by a year on year reduction in the annual numbers of all accidents and minor injury accidents, again this has clearly not been the case, as shown in Figure .

6.5 Conclusion

In this Chapter we complemented our work on the Heinrich triangle by analysing data from a non medication error context in which there were precise definitions of categories. Data of road traffic accidents met these criteria. Using our data display method we can identify interesting trends, however, these do not produce a stable Heinrich ratio. What is seen instead is an illustration of one of the cautionary tales from Chapter 3 (vignette 3) in which an intervention alters the ratio of minor and moderate effects, but does not affect the number of serious events

7 Is there a Heinrich triangle for medication errors? - Conclusions and recommendations

7.1 Answering the research questions

The origin of this project was a request to agree a method of measuring the severity of outcome from medication errors, so that a Heinrich ratio could be calculated. This would allow the estimation of harm resulting from medication errors, and allow the evaluation of initiatives to reduce medication errors. We formalised this in a number of questions which we repeat below, together with the answers found in this report.

1. Is there a Heinrich triangle (ie stable ratio) relating major and minor harm to medication errors?

Response - there is no Heinrich ratio for harm resulting from medication errors. It may be theoretically possible in a very narrow scenario as discussed in Chapter 5, however, there is no evidence for this.

Refutation:

1. *Reviewing the literature on the Heinrich ratio raises serious doubts about the validity and generalisability of the original concept (Chapter 2)*

2. *Logic: the thought experiments in Chapter 3 show that other situations can occur*

3. *Mathematics:*

   a. *the boundaries are extremely sensitive to changes in definitions so that any ratio could be achieved*

   b. *Appendix 3 shows that definitions of medication errors and the ensuing harm are widely different.*

4. *Empirical evidence*

   a. *variability in the ratios for admissions to accident and emergency departments illustrate this for non-drug related data in a medical context (Chapter 4)*

   b. *reconstruction of Heinrich ratios from published papers on medication errors shows significantly different ratios (Chapter 5)*

   c. *systematic changes in ratios over time in data from road traffic accidents show that the Heinrich ratio is not stable in this setting (Chapter 6)*

2. What are the values in the ratio (errors that do not cause harm : minor harm : major harm)?

Response – now not relevant as question 1 above has been refuted

3. Is any change linearly proportional? For example, if the number of errors overall is reduced by 20%, will minor harm and major harm also be reduced by 20%?

Response – not relevant if the ratio is extremely unlikely to exist. Even if it did exist the road traffic accident data suggests that non-linear shifts could occur (Chapter 5).

4. How could we represent this graphically to illustrate and communicate change?

Response – a novel graphical illustration has been created (Chapter 4)

5. How could we show that any change was statistically significant, and not the result of chance? For example, is 247:28:1 significantly different to 312:25:1?

Response – development of 95% confidence regions for the graphical method (Chapter 4)

It is very difficult to show that something does not exist, which is why we have had to use a range of methods and data sets. However, in studying the properties of the Heinrich ratio we conclude that the ratio seems very unlikely to apply to medication errors, and that, even if it did, it seems unlikely to be usable as a method to show that reductions in the number of all errors lead to a proportionate reduction in the number of patients harmed.

This finding is in accord with our experience. We have studied many thousands of medication related acts and errors, and feel that the Heinrich ratio is counter-intuitive. Surely some errors are inherently more dangerous than others; more likely to lead to harm? A single overdose of a vitamin tablet would be much less likely to cause harm than an overdose of an opiate or cytotoxic agent. Errors in drug administration by the intravenous route are more likely to lead to harm than errors in oral or topical administration. Hence initiatives that focus on the types of errors more likely to lead to harm would be expected to produce a greater contribution to safety than reduction in errors that have little potential for harm.

7.2 A way forward

Our findings leave us with the following questions:

First, from our literature review in Appendix 3 it is clear that it is hard to build knowledge and transferable lessons from the literature because of the different lessons and literatures used. In relatively new research areas knowledge is often built from a patchwork of small studies, however this can not be achieved if they are too different. There is a need for better standardisation.

Second, is the causation of medical errors a linear process from which predictions can be made, or is it a system that should be defined "complex" or "chaotic"?

If it is a linear process, can there be a way in which we can predict harm from measurable incidents? For example, is there a way in which one can estimate whether there will be a reduction in harm following initiatives to reduce the incidence of medication errors?

In other words, can the original aim of the project be achieved by other means?

We think this could be achieved by the building of a risk model for medication errors. One of us (SG) has constructed a risk model for error in cardiac surgery which allows the monitoring of individual surgeons to identify whether their surgical outcomes are in the expected range. The building of a model like this in the field of medication errors would be a substantial piece of work. However, we can indicate the sort of issues which we would expect to be in the model. Our experience, the literature on medication errors and the literature on the causes of errors in general would lead us to suggest the following factors:

    1. Therapeutic index of the drug. This is the relationship between the minimum concentration of drug required for the drug to have a clinical effect, and the maximum concentration above which toxic effects appear.

    2. Toxicity of the drug.

    3. Reversibility of error. If an error is detected, how possible is it to reverse, avoid or ameliorate its harmful effects?

    4. The necessity of the drug. This is the extent to which the correct dose of the drug is needed to prevent harm.

    5. The duration of exposure to error.

    6. The resilience of the patient. The extent to which their body is able to cope with an error. Are they relatively healthy when an error occurs, or near death?

    7. The resilience of the systems of work applicable to medicines. The extent to which there are checks and controls to avoid or trap errors and stop them reaching the patient.

    8. Whether the error leads to an increased exposure to a drug, or decreased exposure (or both, as in the case of giving the wrong drug).

We do not know what the elements of a final model would be, nor how well some of the elements could be represented. While much work exists on the prevalence of medication errors and some work on their severity, there is relatively little work on harm and the factors that cause harm. Most evidence of harm comes from incident reports, and commonly refers to the drug and route of administration. However, many factors are not reported and hence it is hard to build a model from this information. As we note in our report on evaluation of electronic prescribing, this issue is crucial for the development of any economic modeling of the consequences of error, and of any interventions to reduce it.

7.3 Research recommendations

We have the following research recommendations:

1. The relationship between errors and harm needs to be further investigated. We have suggested a model built from a combination of the literature, knowledge of pharmacology, logic and understanding of errors in industry. Work is needed to investigate whether our suggested components are suitable predictors of harm from medication errors and whether additional factors are needed. Furthermore, the strength of each individual factor needs to be determined.

2. Our extensive literature review presented in Appendix 3 has shown the many methodological limitations of medication error research. There is an urgent need for a common taxonomy in patient safety research for defining, classifying, measuring and reporting medication incidents. We suggest this is developed as a consensus statement, similar to the CONSORT statement that is widely used for clinical trials.

Word count: 13,972

Acknowledgements

References

(1) Brennan TA, Leape LL, Laird N, Herbert L, Localio AR, Lawthers AG et al. Incidence of adverse events and negligence in hospitalized patients. N Engl J Med 1991; 324(6):370-376.

(2) Wilson RM, Runciman WB, Gibberd RW, Harrison BT, Newby L, Hamilton JD. The quality in Australia health care study. Med J Aust 1995; 163:458-471.

(3) Heinrich HW. Industrial accident prevention. A scientific approach. 1 ed. New York and London: McGraw-Hill Insurance Series; 1931.

(4) Bird FE, Germain GL. Damage Control - A new horizon in accident prevention and cost improvement. Philadelphia: American Management Association; 1966.

(5) Jenman CA. Report on trends in shuttle tanker incidents. London: Health and Safety Executive; 2003.

(6) HMSO. The costs of accidents at work. HSG96 ed. 1993.

(7) Hawkins RD, Fuller CW. Risk assessment in professional football: an examination of accidents and incidents in the 1994 World Cup finals. British Journal of Sports Medicine 1996; 30:165-170.

(8) Hawkins RD, Fuller CW. An examination of the frequency and severity of injuries and incidents at three levels of professional football. British Journal of Sports Medicine 1998; 32:326-332.

(9) Jones S, Kirchsteiger C, Bjerke W. The importance of near miss reporting to further improve safety performance. Journal of Loss Prevention in the Process Industries 1999; 12:59-67.

(10) Bird FE, Germain GL. Practical loss control leadership. Revised Edition ed. Logainville, USA: Det Norske Veritas; 1996.

(11) Uth HJ, Wiese N. Central collecting and evaluating of major accidents and near-miss-events in the Federal Republic of Germany - results, experiences, perspectives. Journal of Hazardous Materials 2004; 111:139-145.

(12) Bureau of Transportation Statistics. Project 7 Overview - Expand the collection of "near-miss" data to all modes. www.bts.gov (accessed 29.07.2004): Department of Transportation, USA; 2004.

(13) Barton R, Bergeron J, Marchand R. How to implement incentive programs for safety and productivity: guidelines for transport fleets. Transport Canada TP 13805E; 2001.

(14) Phimister JR, Oktem U, Kleindorfer PR, Kunreuther H. Near-miss incident management in the chemical process industry. Risk Analysis 2003; 23(3):445-459.

(15) Department of Health. Building a safer NHS for patients - Improving medication safety. London: Department of Health; 2004.

(16) Audit Commission for Local Authorities and the National Health Service in England and Wales. A spoonful of sugar - medicines management in NHS hospitals. London: Audit Commission; 2001.

(17) Meyer G, Heigel FJ, Flink E. Error reporting systems - A workshop for state patient safety "teams": Nashville, Tenessee, USA. In: Agency for Healthcare Research and Quality, editor. Beyond state reporting: medical errors and patient safety issues. www.ahrq.gov/news/ulp/patsafety/ptsafety7.htm: 2001.

(18) Bion JF, Heffner JE. Challenges in the care of the acutely ill. Lancet 2004; 363:970-977.

(19) Furukawa H, Bunko H, Tsuchiya F, Miyamoto K. Voluntary medication error reporting program in a Japanese national university hospital. Annals of Pharmacotherapy 2003; 37:1716-1722.

(20) Kaplan H. Lessons learned. Transfusion 2001; 41:575-576.

(21) Wadman MC, Muellemann RL, Coto JA, Kellermann AL. The pyramid of injury: using ecodes to accurately describe the burden of injury. Annals of Emergency Medicine 2003; 42:468-478.

(22) Silverman D. Interpreting qualitative data: methods for analysing talk, text and interaction. 1 ed. London: Sage; 1993.

(23) Reason J. Human error. 1 ed. Cambridge: Cambridge University Press; 1990.

(24) Dean B, Schaechter M, Vincent C, Barber N. Causes of prescribing errors in hospital inpatients: a prospective study. Lancet 2002; 359:1373-1378.

(25) Taxis K, Barber N. Ethnographic study of incidence and severity of intravenous drug errors. Brit Med J 2003; 326:684-687.

(26) Wright L, Van der Schaaf T. Accident versus near miss causation: a critical review of the literature, an empirical test in the UK railway domain, and their implications for other sectors. Journal of Hazardous Materials 2004; 111:105-110.

(27) Heinrich HW. Industrial accident prevention. A safety management approach. 5 ed. New York: McGraw-Hill; 1980.

(28) Bates DW, Boyle DL, Vander Vliet M, Schneider J, Leape LL. Relationship between medication errors and adverse drug events. J Gen Int Med 1995; 10:199-205.

(29) Kaushal R, Bates DW, Landrigan C, McKenna C, Clapp MD, Federico F et al. Medication errors and adverse drug events in pediatric inpatients. JAMA 2001; 285:2114-2120.

(30) Dean B, Schachter M, Vincent C, Barber N. Prescribing errors in hospital inpatients: their incidence and clinical significance. Qual Saf Health Care 2002; 11:340-344.

(31) Lesar TS, Briceland L, Stein DS. Factors related to errors in medication prescribing. JAMA 1997; 277:312-317.

(32) Dean B, Barber N. The effects of a patient's own drugs scheme on the incidence and severity of medication administration errors. Int J Pharm Pract 2000; 8:209-216.

(33) Dean BS, Barber ND. A validated, reliable method of scoring the severity of medication errors. Am J Health-Syst Pharm 1999; 56:57-62.

(34) Taxis K, Barber N. Incidence and severity of intravenous drug errors in a German hospital. Eur J Clin Pharmacol 2004; 59(11):815-817.

(35) Taxis K, Dean B, Barber N. The validation of an existing method of scoring the severity of medication administration errors for use in Germany. Pharm World Sci 2002; 24:236-239.

(36) van den Bemt PMLA, Fijn R, van der Voort PHJ, Gossen AA, Egberts TCG, Brouwers JRBJ. Frequency and determinants of drug administration errors in the intensive care unit. Critical Care Medicine 2002; 30(4):846-850.

(37) Hartley GM, Dhillon S. An observational study of the prescribing and administration of intravenous drugs in a general hospital. Int J Pharm Pract 1998; 6:38-45.

(38) Tissot E, Cornette C, Demoly P, Jacquet M, Barale F, Capellier G. Medication errors at the administration stage in an intensive care unit. Intensive Care Medicine 1999; 25:353-359.

(39) Stucky ER. Prevention of medication errors in the pediatric inpatient setting. Pediatrics 2003; 112(2):431-436.

(40) Bates DW, Cullen DJ, Laird N, Petersen LA, Small SD, Servi D et al. Incidence of adverse drug events and potential adverse drug events. JAMA 1995; 274(1):29-34.

(41) Transport Statistics. Transport Statistics Bulletin - Road casualties in Great Britain. SB (04) 30 (available at www.dft.gov.uk) ed. Crown Copy Right; 2004.

(42) Armitage P, Berry G. Statistical methods in medical research. 3 ed. Oxford: Blackwell Science; 1994.

(43) Moher D, Schulz K, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. Lancet 2001; 357:1191-1194.

(44) Barber N. Should we consider non-compliance a medical error? Qual Saf Health Care 2002; 11(1):81-84.

(45) Barker KN, Kimbrough WW, Heller WM. A study of medication errors in a hospital. University of Arkansas, Fayetteville, Arkansas; 1966.

(46) Bates DW, Gawande AA. Improving safety with information technology. N Engl J Med 2003; 348:2526-2534.

(47) Gandhi TK, Weingart SN, Borus J, Seger AC, Peterson J, Burdick E et al. Adverse drug events in ambulatory care. N Engl J Med 2003; 348(16):1556-1564.

(48) Ashcroft DM, Quinlan P, Blenkinsopp A. Prospective study of the incidence, nature and causes of dispensing errors in community pharmacies. Pharmacoepidemiol Drug Saf 2005; 14(5):327-332.

(49) Allan EL, Barker KF, Malloy MJ, Heller WM. Dispensing errors and counseling in community practice. American Pharmacy 1995; NS35(12):25-32.

(50) Dean Franklin B, Vincent C, Schachter M, Barber N. Prescribing errors - an overview of research methods. Drug Safety (in press) 2005.

(51) anonymous. Suggested definitions and relationships among medication misadventures, medication errors, adverse drug events, and adverse drug reactions. Am J Health-Syst Pharm 1998; 55:165-166.

(52) van den Bemt PMLA, Egberts TCG, de Jong-van den Berg LTW, Brouwers JRBJ. Drug-related problems in hospitalised patients. Drug Safety 2000; 22(4):321-333.

(53) Institute of Medicine Committee on the Quality of Health Care in America. To err is human. Washington: National Academy Press; 2000.

(54) Winterstein AG, Johns TE, Rosenberg EI, Hatton RC, Gonzalez-Rothi R, Kanjanarat P. Nature and causes of clinically significant medication errors in a tertiary care hospital. Am J Health Syst Pharm 2004; 61(18):1908-1916.

(55) Lilford RJ, Mohammed MA, Braunholtz D, Hofer TP. The measurement of active errors: methodological issues. Qual Saf Health Care 2003; 12 Suppl 2:ii8-12.

(56) Dean B, Barber N, Schachter M. What is a prescribing error? Qual Health Care 2000; 9:232-237.

(57) Sagripanti M, Dean B, Barber N. An evaluation of the process-related medication risks for elective surgery patients from pre-operative assessment to discharge. Int J Pharm Pract 2002; 10:161-170.

(58) Haw C, Stubbs J. Prescribing errors in a psychiatric hospital. Pharmacy in Practice 2003; 23:64-66.

(59) Tuthill A, Wood K, Cavell GF. An audit of drug allergy documentation on inpatient drug charts. Pharm World Sci 2004; 26:a48-a49.

(60) Lawler C, Welch S, Brien JE. Omitted medication doses: frequency and severity. Journal of Pharmacy Practice and Research 2004; 34:174-177.

(61) Fijn R, van den Bemt PMLA, Chow M, De Blaey CJ, de Jong-van den Berg LTW, Brouwers JRBJ. Hospital prescribing errors: epidemiological assessment of predictors. Br J Clin Pharmacol 2002; 53:326-331.

(62) Potts AL, Barr FE, Gregory DF, Wright L, Patel NR. Computerized physician order entry and medication errors in a pediatric critical care unit. Pediatrics 2004; 113(1 Pt 1):59-63.

(63) Lesar TS, Lomaestro BM, Pohl H. Medication-prescribing errors in a teaching hospital. Arch Intern Med 1997; 157:1569-1576.

(64) Folli HL, Poole RL, Benitz WE, Russo JC. Medication error prevention by clinical pharmacists in two children's hospitals. Pediatrics 1987; 79:718-722.

(65) Blum K, Abel SR, Urbanski CJ, Pierce JM. Medication error prevention by pharmacists. Am J Hosp Pharm 1988; 45:1902-1903.

(66) anonymous. ASHP Standard definition of a medication error. Am J Hosp Pharm 1982; 39:321.

(67) Allan Flynn E, Barker KN. Medication errors research. In: Cohen MR, editor. Medication errors. Washington: American Pharmaceutical Association; 1999. 6.1-6.30.

(68) Lacasa C, Cot R, Roure C, Martinez J, Polo C, Andreu C et al. Medication errors in a general hospital. Eur Hosp Pharm 1998; 4(2):35-40.

(69) Gethins B. Wise up to medication errors. Pharmacy in Practice 1996;323-328.

(70) Baker HM. Rules outside the rules for administration of medication: A study in New South Wales, Australia. Journal of Nursing Scholarship 1997; 29(2):155-158.

(71) Tamuz M, Thomas EJ, Franchois KE. Defining and classifying medical error: lessons for patient safety reporting systems. Qual Saf Health Care 2004; 13:13-20.

(72) World Health Organisation. International drug monitoring: the role of national centres. Geneva, Switzerland: World Health Organisation; 1972.

(73) World Health Organisation. Safety of medicines. WHO/EDM/QSM/2002.2 ed. Geneva: World Health Organisation; 2002.

(74) anonymous. Safety monitoring of medicinal products. Uppsala, Sweden: Uppsala Monitoring Centre, World Health Organisation Collaborating Centre for International Drug Monitoring; 2000.

(75) Beijer HJM, De Blaey CJ. Hospitalisations cause by adverse drug reactions (ADR): a meta-analysis of observational studies. Pharm World Sci 2002; 24(2):46-54.

(76) Wiffen P, Gill M, Edwards J, Moore A. Adverse drug reactions in hospital patients. Bandolier Extra 2002; June:1-15.

(77) McDonnell PJ, Jacobs MR. Hospital admissions resulting from preventable adverse drug reactions. Annals of Pharmacotherapy 2002; 36:1331-1336.

(78) The National Reporting and Learning System Service dataset Acute / General Hospital 2003/4 Release 1.2.0. National Patient Safety Agency, editor. 2004. www.npsa.nhs.uk (accessed 5.1.2005).

(79) Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients. JAMA 1998; 279(15):1200-1205.

(80) Bates DW, Leape LL, Petrycki S. Incidence and preventability of adverse drug events in hospitalized adults. J Gen Int Med 1993; 8:289-294.

(81) Irey NS. Adverse drug reactions and death. JAMA 1976; 236(6):575-578.

(82) Porter J, Jick H. Drug-related deaths among medical inpatients. JAMA 1977; 237:879-881.

(83) Miller RR. Hospital admissions due to adverse drug reactions. Arch Intern Med 1974; 134:219-223.

(84) anonymous. Potential for confusion between Lamictal and Lamisil. Current problems in pharmacovigilance 1997; 23:14.

(85) anonymous. Medication error: potential for confusing Humalog and Humalog Mix 25. Current problems in pharmacovigilance 2000; 26:4.

(86) anonymous. Reminder: Methotrexate safe prescribing and dispensing. Current problems in pharmacovigilance 2000; 26:10.

(87) anonymous. Accidental overdose with alfacalcidol (One-Alpha drops). Current problems in pharmacovigilance 2001; 21:3.

(88) Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis and management. Lancet 2000; 356:1255-1259.

(89) Note for guidance on clinical safety data management: defintions and standards for expedited reporting (CPMP/ICH/377/95). The European Agency for the evaluation of medicinal products, editor. 1994. http://www.eudravigilance.org/human/docs/e2a.pdf.

(90) Post-approval safety data management? definitions and standards for expedited reporting E2D. International Conference on Harmonisation of technical requirements for registration of pharmaceuticals for human use, editor. 2003.

(91) Meyler L. Foreword. Side effects of drugs 1955-1956. Amsterdam: The Excerpta Medica Foundation; 1957. 1.

(92) Meyler L. Foreword. Side effects of drugs 1960. 3 ed. Amsterdam: Excerpta Medica Foundation; 1960.

(93) Caranasos GJ, Stewart RB, Cluff LE. Drug-induced illness leading to hospitalization. JAMA 1974; 228:713-717.

(94) Caranasos GJ, May FE, Stewart RB, Cluff LE. Drug-associated deaths of medical inpatients. Arch Intern Med 1976; 136:872-875.

(95) Gurwitz JH, Field TS, Harrold LR, Rothschild J, Debellis K, Seger AC et al. Incidence and preventability of adverse drug events among older persons in the ambulatory setting. JAMA 2003; 289(9):1107-1116.

(96) Leape LL, Brennan TA, Laird N, Lawthers AG, Localio AR, Barnes BA et al. The nature of adverse events in hospitalized patients. N Engl J Med 1991; 324:377-384.

(97) Field TS, Gurwitz JH, Avorn J, McCormick D, Jain S, Eckler M et al. Risk factors for adverse drug events among nursing home residents. Arch Intern Med 2001; 161(13):1629-1634.

(98) Nebeker JR, Hoffman JM, Weir CR, Bennett CL, Hurdle JF. High rates of adverse drug events in a highly computerized hospital. Arch Intern Med 2005; 165(10):1111-1116.

(99) Holdsworth MT, Fichtl RE, Behta M, Raisch DW, Mendez-Rico E, Adams A et al. Incidence and impact of adverse drug events in pediatric inpatients. Arch Pediatr Adolesc Med 2003; 157(1):60-65.

(100) Kucukarslan SN, Peters M, Mlynarek M, Nafziger DA. Pharmacists on rounding teams reduce preventable adverse drug events in hospital general medicine units. Arch Intern Med 2003; 163:2014-2018.

(101) Classen DC, Pestotnik SL, Evans RS, Burke JP. Computerized surveillance of adverse drug events in hospital patients. JAMA 1991; 266(20):2847-2851.

(102) Classen DC, Pestotnik SL, Evans RS, Lloyd JF, Burke JP. Adverse drug events in hospitalized patients. JAMA 1997; 277(4):301-305.

(103) Ahmad SR. Adverse drug event monitoring at the Food and Drug Administration. J Gen Int Med 2003; 18:57-60.

(104) Smith J. Building a safer NHS for patients - Improving medication safety. London: Department of Health; 2004.

(105) Department of Health. An organisation with a memory. London: The Stationery Office; 2000.

(106) Aspden P, Corrigan JM, Wolcott J, Erickson SM. Patient Safety: Achieving a New Standard for Care. Washington: Institute of Medicine; The National Academies Press; 2004.

(107) Glossar of the National Center for Patient Safety (NCPS) of the Veteran Health Administration, USA. http://www.patientsafety.gov/index.html accessed on 6.09.2005 . 2005.

(108) Thomas EJ, Petersen LA. Measuring Errors and Adverse Events in Health Care. J Gen Int Med 2003; 18(1):61-67.

(109) Neale G, Woloshynowych M, Vincent C. Exploring the causes of adverse events in NHS hospital practice. Journal of the AI Association 2001.

(110) Phillips DP, Christenfeld N, Glynn LM. Increase in US medication-error deaths between 1983 and 1993. Lancet 1998; 351:643-650.

(111) Lesar TS, Briceland L, Delcoure K, Parmalee JC, Masta-Gornic V, Pohl H. Medication prescribing errors in a teaching hospital. JAMA 1990; 263:2329-2334.

(112) Tesh DE, Beeley L. Errors of drug prescribing. Br J Clin Pharmacol 1975; 2(5):403-409.

(113)   Thomas EJ, Brennan TA. Incidence and types of preventable adverse events in elderly patients: population based review of medical records. Brit Med J 2000; 320:741-744.

(114)   Vincent C, Neale G, Woloshynowych M. Adverse events in British hospitals: preliminary retrospective record review. Brit Med J 2001; 322:517-519.

(115)   Hayward RA, Hofer TP. Estimating hospital deaths due to medical errors. JAMA 2001; 286(4):415-420.

(116)   Rozich JD, Haraden CR, Resar RK. Adverse drug event trigger tool: a practical methodology for measuring medication related harm. Qual Saf Health Care 2003; 12(3):194-200.

(117)   Burke R, Timmins J, Wilkins J, Doyle B. The use of trigger tools to detect adverse drug events in an Australian hospital. Abstract presented at Society of Hospital Pharmacists of Australia, Cranberra, November 2003 2003.

(118)   Honigman B, Lee J, Rothschild J, Light P, Pulling RM, Yu T et al. Using computerized data to identify adverse drug events in outpatients. J Am Med Inform Assoc 2001; 8(3):254-266.

(119)   Phelps CE. The methodological foundations of studies of the appropriateness of medical care. N Engl J Med 1994; 329:1241-1245.

(120)   Phillips I, Eykyn S, Laker M. Outbreak of hospital infection caused by contaminated autoclaved fluids. Lancet 1972; i:1258-1260.

(121)   Ferner RE, Whittington RM. Coroner's cases of death due to errors in prescribing of giving medicines or to adverse drug reactions: Birmingham 1986-1991. Journal of the Royal Society of Medicine 1994; 87:145-148.

(122)   Jha AK, Kuperman GJ, Teich JM, Leape L, Shea B, Rittenberg E et al. Identifying adverse drug events: development of a computer-based monitor and comparison with chart review and stimulated voluntary report. J Am Med Inform Assoc 1998; 5(3):305-314.

(123)   Raschke RA, Gollihare B, Wunderlich TA, Guidry JR, Leibowitz AI, Peirce JC et al. A computer alert system to prevent injury from adverse drug events. JAMA 1998; 280(15):1317-1320.

(124)   Payne TH, Savarion J, Marshall R, Hoey CT. Use of a clinical event monitor to prevent and detect medication errors. Proc AMIA Annu Fall Symp 2000;(640):644.

(125)   Hawkey CJ, Hodgson S, Norman A, Daneshmend TK, Garner ST. Effect of reactive pharmacy intervention on quality of hospital prescribing. BMJ 1990; 300(6730):986-990.

(126)   Barber ND, Batty R, Ridout D. Predicting the rate of physician-accepted interventions by the hospital pharmacists in the United Kingdom. Am J Health-Syst Pharm 1997; 54(February 15):397-404.

(127) McFadzean E, Isles C, Moffat J, Norrie J, Stewart D. Is there a role for a prescribing pharmacist in preventing prescribing errors in a medical admissions unit? Pharm J 2003; 270:896-899.

(128) Barker KN, McConnell WE. Detecting errors in hospitals. Am J Hosp Pharm 1962; 19:361-369.

(129) Barber ND, Dean B. The incidence of medication errors and ways to reduce them. Clinical Risk 1998; 4:103-106.

(130) Clark CM, Bailie GR, Whitaker AM, Goldberg LA. Parenteral drug delivery - value for money? Pharm J 1986; 236(April 12):453-455.

(131) O'Hare MCB, Gallagher T, Shields MD. Errors in the administration of intravenous drugs. BMJ 1995; 310:1536-1537.

(132) Wirtz V, Taxis K, Barber N. An observational study of intravenous medication errors in the United Kingdom and in Germany. Pharm World Sci 2003; 25:104-111.

(133) NCC MERP Taxonomy of Medication Errors. 1998. http://www.nccmerp.org/pdf/taxo2001-07-31.pdf (accessed 4.1.2005), National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP).

(134) Taxis K, Dean B, Barber N. Hospital drug distribution systems in the UK and Germany, a study of medication errors. Pharm World Sci 1999; 21:25-31.

(135) Dean B, Barber N. Validity and reliability of observational methods for studying medication administration errors. Am J Health-Syst Pharm 2001; 58:54-59.

(136) Ferner RE, Langford NJ, Anton C, Hutchings A, Bateman DN, Routledge PA. Random and systematic medication errors in routine clinical practice: a multicentre study of infusions, using acetylcysteine as an example. Br J Clin Pharmacol 2001; 52:573-577.

(137) Allan Flynn E, Barker KN, Pepper GA, Bates DW, Mikeal RL. Comparison of methods for detecting medication errors in 36 hospitals and skilled nursing facilities. Am J Health-Syst Pharm 2002; 59:436-446.

(138) Ross LM, Wallace J, Paton JY. Medication errors in a paediatric teaching hospital in the UK: five years operational experience. Arch Dis Child 2000; 83:492-497.

(139) Bruce J, Wong I. Parenteral drug administration errors by nursing staff on an acute medical admissions ward during day duty. Drug Safety 2001; 24(11):855-862.

(140) Hall KW, Ebbeling P, Brown B, Shwortz I. A retrospective-prospective study of medication errors: basis for an ongoing monitoring program. Can J Hosp Pharm 1985; 38(5):141-3, 146.

(141) McNally KM, Sunderland B. No-blame medication administration error reporting by nursing staff at a teaching hospital in Australia. Int J Pharm Pract 1998; 6:67-71.

(142) van den Bemt PMLA, Postma MJ, van Roon EN, Chow M-CC, Fijn R, Brouwers JRBJ. Cost-benefit analysis of the detection of prescribing errors by hospital pharmacy staff. Drug Safety 2002; 25(2):135-143.

(143) Simborg DW, Derewicz HJ. A highly automated hospital medication system. Annals of Internal Medicine 1975; 83:342-346.

(144) Kozer E, Scolnik D, Macpherson A, Keays T, Shi K, Luk T et al. Variables associated with medication errors in pediatric emergency medicine 2. Pediatrics 2002; 110(4):737-742.

(145) King WJ, Paice N, Rangrej J, Forestell GJ, Swartz R. The effect of computerized physician order entry on medication errors and adverse drug events in pediatric inpatients. Pediatrics 2003; 112:506-509.

(146) Hynniman CE, Conrad WF, Urch WA, Rudnick BR, Parker PF. A comparison of medication errors under the University of Kentucky unit dose system and traditional drug distribution systems in four hospitals. Am J Hosp Pharm 1970; 27:802-814.

(147) Tisdale JE. Justifying a pediatric critical-care satellite pharmacy by medication-error reporting. Am J Hosp Pharm 1986; 43:368-371.

(148) Tyndall LL, Carlson SA. Use of an objective rating scale to evaluate medication errors. ASHP Annual Meeting 1990; 47:22.

(149) Dean B. Hospital medication administration errors - their simulation, observation and severity assessment. University of London; 1999.

(150) Peyriere H, Cassan S, Floutard E, Riviere S, Blayac J-P, Hillaire-Buys D et al. Adverse drug events associated with hospital admission. Annals of Pharmacotherapy 2003; 37:5-11.

(151) Moclair AE, Hecker JF, Willson A, Bates IP. Prolonging the survival of peripheral infusion sites in neonates with low dose heparin. The International Journal of Pharmacy Practice 1992; 1(Aug):198-201.

(152) van den Bemt PMLA, Egberts ACG. Bijwerkingen en medicatiefouten systematisch ingedeeld. Pharmaceutisch Weekblad 2002; 137(44):1540-1543.

(153) Beyer M, Gerlach FM. Medikationsfehler in deutschen Allgemeinpraxen - eine Forschungsnotiz. Zeitschrift für Allgemeinmedizin 2003; 79:332-335.

Appendix 1: Mathematical proof accompanying section 0

Let f denote a continuous probability distribution function whose non-zero values occur within the interval [u,w], which might be an unbounded interval. Then the following is easy to establish:

Theorem

If A, B and C are positive real numbers that sum to 1, then there exist category boundary values v_1 and v_2 such that

$$\int_{u}^{v_1} f(z)dz = A$$

$$\int_{v_1}^{v_2} f(z)dz = B$$

and

$$\int_{v_2}^{w} f(z)dz = C.$$

Proof

Consider the cumulative distribution function *g(x)* defined on the interval *[u,w]* given by

$$g(x) = \int_{u}^{x} f(z)dz$$

Clearly *g(u)=0* and, since *f* is a probability distribution, g(w)=1.

Also, within the interval *[u,w]*, *g* is differentiable with

$$\frac{dg}{dx}(x) = f(x) > 0.$$

Thus the function g is continuous and strictly increasing.

In view of this, the value v_1 corresponds to the (unique) value of *x* where *g(x)=A* and v_2 corresponds to the (unique) value of *x* where *g(x)= 1-A-B.*

This result implies that under very general terms, if outcomes are continuous, and subdivided into three categories by arbitrary boundary values, then it is possible to achieve any Heinrich ratio, depending how these boundary values are chosen.

Appendix 2: Mathematical details accompanying chapter 4

Mathematical details concerning derivation of coordinates for plotting data points within an equilateral triangle and constructing approximate confidence regions around those data points (accompanying Chapter 4)

Derivation of coordinates for the data points

It should be noted that the vector representing a data point in T is the weighted vector sum of the three vectors corresponding to the three vertices of the triangle, the weights simply being the three relative proportions. In order to visualise a data point in two dimensional space, one simply needs to take the corresponding weighted vector sum of the vectors representing the vertices of an equilateral triangle. Any equilateral triangle serves this purpose, however it is useful to use the triangle with

vertices: $\mathbf{v}_1 = (0,1)$, $\mathbf{v}_2 = (-\frac{\sqrt{3}}{2}, -\frac{1}{2})$ and $\mathbf{v}_3 = (\frac{\sqrt{3}}{2}, -\frac{1}{2})$.

Thus if a given study reports x no harm incidents, y minor incidents and z major incidents, then these data are represented by the point:

$$\frac{z}{x+y+z}\mathbf{v}_1 + \frac{x}{x+y+z}\mathbf{v}_2 + \frac{y}{x+y+z}\mathbf{v}_3.$$

which can be expressed as the two dimensional vector

$$\frac{1}{x+y+z}\left(\frac{\sqrt{3}(y-x)}{2}, \frac{2z-y-z}{2}\right).$$

This is shown in Figure 26
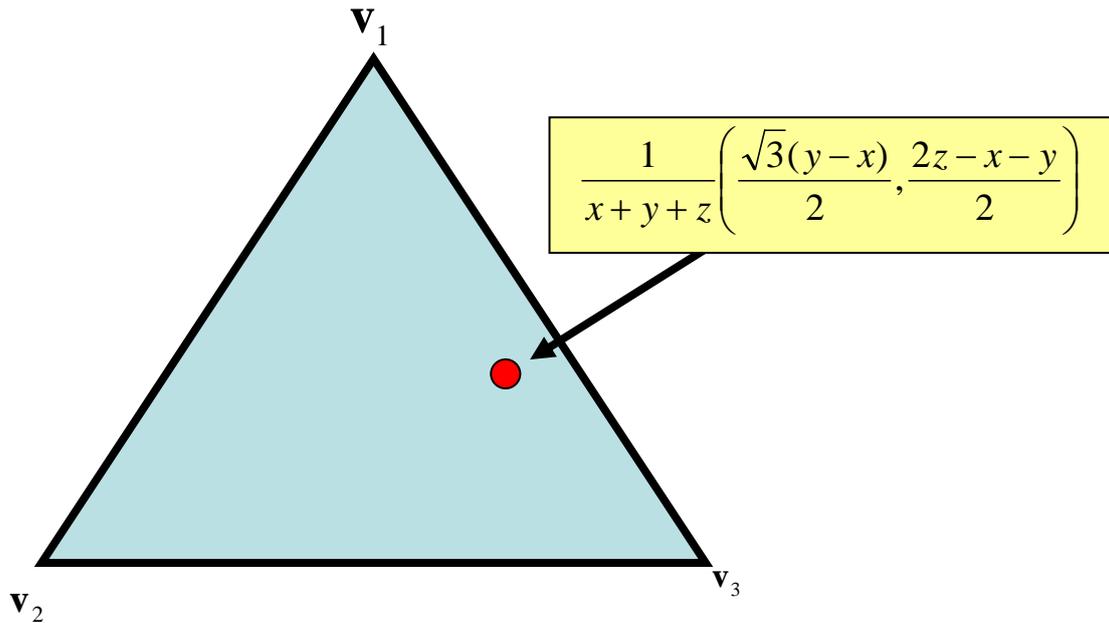
Figure 26: Representing three relative frequencies as a point within an equilateral triangle in two dimensional space.

It should be noticed in passing that if x=y=z, then the data point is represented as the centroid of the triangle, as one would expect.

Approximate confidence regions

The graphical technique discussed above can be enhanced by superimposing a region around the data point corresponding to a 95% confidence interval. Precise estimation of the boundary of such a region using exact statistical methods is somewhat complex. Alternatively, an approximate confidence region can be constructed as follows:

Standard statistical methods exist for calculating 95% confidence intervals for the estimate of a proportion of events that fall into one of two categories. For example, if sample sizes are not too small and if the estimated proportions are not close to either zero or one, then an approximate 95% confidence interval is given by:

$$p \pm 1.96 \sqrt{\frac{p(1-p)}{N}}$$

Where N is the number of observations and p is the estimated proportion

If sample sizes are small, or if the proportion estimates are close to zero or one, then exact statistical methods [42] can be used to get precise estimates for the confidence intervals, although these are more difficult to express in terms of mathematical formulae.

Using these estimation methods, one can calculate a confidence interval for the relative proportions of major and minor incidents. Equally, one can derive a confidence interval for the relative proportions of minor and no-harm incidents and can repeat this process for major and no-harm incidents.

Having done this, the geometric method shown in Figure 27 illustrates how these three confidence intervals can be used to derive a polygonal confidence region around the data point used to represent a survey's findings.
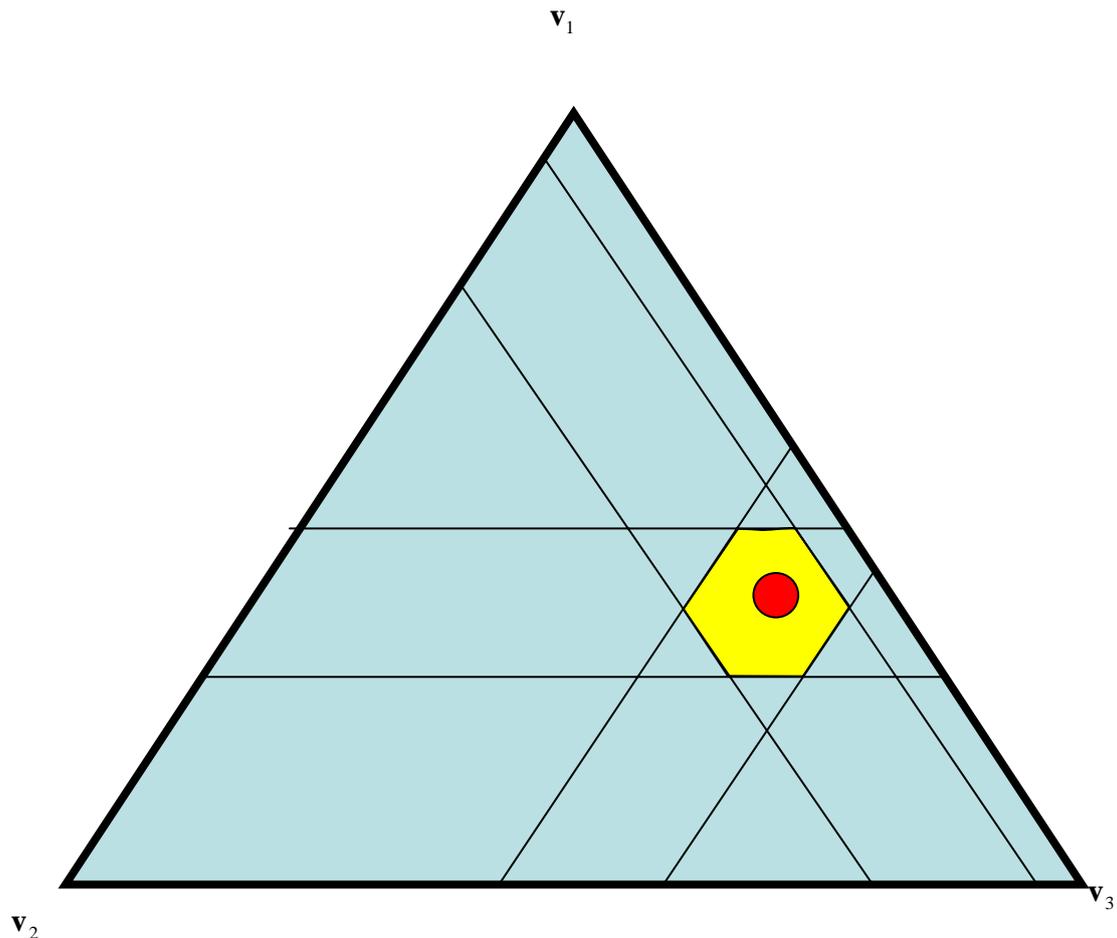
Figure 27: Using confidence intervals for relative proportions considered two at a time to infer a confidence region for the relative proportions of three quantities.

Confidence interval contours

The polygonal region used in the previous section has a subtle statistical deficiency in that it is based on considering sets of events in pairs rather than using all the data simultaneously, whereas in principle, one should construct a confidence region using a joint multinomial distribution based on all of the data. For large sample sizes, this can be achieved using maximum likelihood methods.

There is only a slight difference between the polygonal approximation and the maximum likelihood estimated contour as illustrated below (Figure 28).
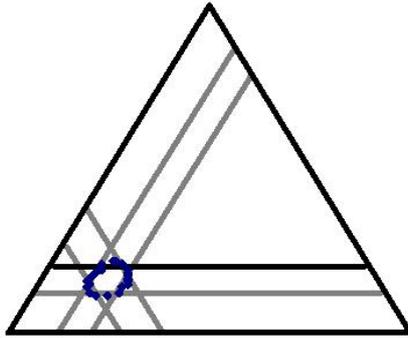
Figure 28: Comparison of 95% contour region derived from multinomial distribution and polygonal approximation (data in ratio 50:50:200)

Appendix 3: A commentary on medication error definitions, research methods and severity assessment

1. Background

In this project we investigated whether there is a Heinrich triangle for medication errors. The basis of the Heinrich triangle is to classify events in three categories of outcome (no harm accidents/moderate injuries /major injuries). However, many studies of errors have not assessed severity, but have instead counted all errors equally. Others have attempted to assess severity in a variety of ways based on actual outcome, expert judgement of potential outcome or on proxy indicators of severity. This leads to the more fundamental question of *which events should be classified as medication errors* (i.e., what is the definition of a medication error) and what is the difference between a medication error and an adverse drug event, an adverse drug reaction, a near miss incident, to name but a few of the terms that are used to describe medication incidents.

These issues of definitions are closely related to the methods that are used to obtain data on medication errors. The results of medication error research are very sensitive to changes in definitions, methods, and assessment of ensuing harm. These differences can lead to reports of medication error rates that are orders of magnitude apart and make it very difficult to compare different studies. For any result of a study to be used to establish a Heinrich ratio we need to consider the mentioned issues.

Complementary to the main body of this report we therefore attempt to make sense of the diverse literature on medication errors. We investigate the following three issues:

- definitions of medication errors, and how these are related to other terms used in the area (adverse drug reactions, adverse drug event, adverse event etc).
- methods used to measure medication error rates, highlighting their strengths and limitations
- methods used to assess the (potential) outcome of medication errors, highlighting their strengths and limitations

However, this section is not only to be seen in the context of investigating the Heinrich ratio of medication errors; we think the results presented in this section have wider implications. In the area of medication error research, we find a general

lack of standard definitions and methods. Even more problematic is the poor standard of reporting definitions and methods in research studies. This makes it difficult sometimes impossible to assess the generalisability of research. There is an urgent need to establish standards for conducting and reporting medication error research. Such standards have been successfully developed for clinical trials of drugs (the "CONSORT statement") [43] and it is high time for similar action in research of patient safety incidents involving drug use. The following review is therefore also a basis for the development of such standards.

2. Data sources

A literature search in Pubmed, International Pharmaceutical Abstracts, EMBASE and our own database of literature was carried out in February/March 2004 with an update in June 2005. This was complemented by a hand search in relevant libraries for early material on adverse drug reactions (for example, in the library of the Royal Society of Medicine). Furthermore, the cited references of relevant articles were carefully studied to identify further references. Search terms included medication errors, adverse drug reaction, adverse drug event.

3. Definitions of medication incident
3.1 Terms used to describe medication incidents and the schools of thought using them

Terms that are most commonly used to describe incidents that involve medication use are:
- medication errors
- patient safety incident involving medicines
- adverse drug reactions
- adverse drug events
- adverse events
- inappropriate prescribing/drug related problems

Furthermore, non-compliance of patients could be also considered a medical or medication error,[44] but this is outside the scope of the present report.

A shift in terminology can be observed in recent years to avoid the word "error" and use "safety" instead. For example the terms, "patient safety research" or "patient safety incidents" are used frequently. Consequently, the NPSA uses the term "patient

safety incident involving drug use" as a synonym for medication errors, although safety and error are two different concepts.

Broadly the events fall into two categories:
- deviations from defined/established processes of drug use regardless of their outcome (medication errors, patient safety incidents involving drug use)
- harmful events and the role of medicines in their cause (adverse drug reactions, adverse drug events, adverse events).

In order to understand difference and overlap of definitions, it may be helpful to look at the disciplines or schools of thought from which these terms are derived (Table 9)

Discipline/school of thought	Aims	Terms
Pharmacovigilance / Pharmacoepidemiology	Pre- and postmarketing surveillance of drugs to establish risk profile for each drug	Adverse drug reactions
Medication error research; Health and safety; Systems process management; Psychology of behaviour	Analysis of the incidence and causes of medication errors	Medication errors, patient safety incidents involving drug use, adverse drug event, near miss
Clinical trials	Assessment of efficiency/effectiveness/safety of individual drugs	Adverse events
Quality assurance/management	Quality improvement	Inappropriate prescribing/drug related problems

Table 9: Overview of the terms used by the different disciplines/schools of thought investigating medication incidents

The disciplines pharmacovigilance and pharmacoepidemiology are traditionally concerned with studying adverse drug reactions with the aim of describing the individual risk profile of each drug. Adverse drug reactions are thus the characteristics of a drug and can be largely explained by its pharmacological properties and the interactions between drug and human body. Much of the research and in particular the regulation in the area of pharmacovigilance was triggered by the discovery of the foetal malformation due to thalidomide. Methods to obtain information on adverse drug reactions include clinical trials and spontaneous adverse drug reaction reporting systems (such as the Yellow Card Scheme in the UK). The term adverse event is used in the context of clinical trials.

The medication error research community is concerned with assessing the risks of drug use in practice, studying the processes including prescribing, dispensing, preparing and administration of medicines, and identifying the failures and faults in these systems. Terms used include medication errors, adverse drug events, inappropriate prescribing. Early research in this area assessed the error rates associated with different drug distribution systems.[45] More recently, a lot of research efforts are around the incidence and causes of prescribing errors in hospital [30] and the impact of electronic prescribing systems on medication errors and adverse drug events.[46] The majority of this research has been carried out in secondary care. Fewer studies looked at the situation of medication errors in ambulatory care [47] or investigated dispensing errors in community pharmacies.[48;49] As we have already highlighted, there is a shift to call research in this area patient safety research (but this term encompasses not only medication related processes, but other medical processes as well) or medication safety research if referring to medication related activities only.

These two traditions of thought have different views on the causes of harm and hence different research methods. Within pharmacovigilance / pharmacodepidemiology the drug is seen as the cause of harm and there is little review of the process. Medication error researchers see the failure of the system as causes of harm and hence are interested in what people do.

There is a body of research around *inappropriate prescribing* or *drug related problems* in primary and secondary care. There is some overlap between these terms and medication errors. Some of the events considered to be inappropriate prescribing could be also called medication errors and likewise medication errors can result in drug related problems. In general, research in the area of quality management is wider than medication error research. An in-depth review of the literature on inappropriate prescribing/drug related problems is outside the scope of the present report.
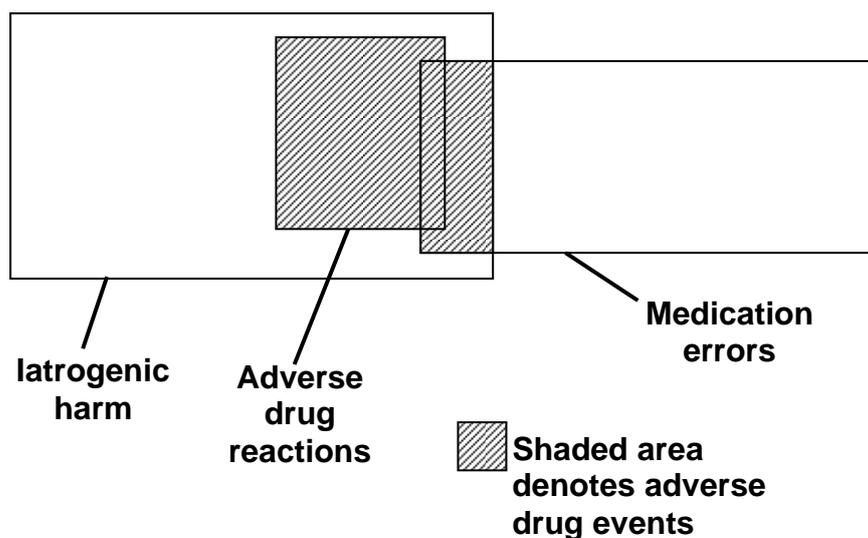
Figure 29: Relationships between medication errors and different types of iatrogenic injury (from [50])

Figure 29 is a graphical illustration of how we see the relationships between medication errors and different types of iatrogenic injury.[50] However, reviewing research reports, meta-analysis, literature reviews, and government documents we find that different meanings are attached to these terms. In the following we describe the different definitions and how they are understood and used in practice. The focus of this report is on medication errors. Therefore for terms such as adverse drug reactions we explore the extent to which these terms may also encompass medication errors.

3.2 Definitions describing deviations from process of drug use

Medication errors/patient safety incidents involving medicines
Medication errors have been defined in many different ways. Some of the definitions relate to all types of medication errors, others relate to specific types of errors, eg. prescribing errors and administration errors. Reviewing the definition we find that these are either based on

- explicit criteria of what is considered erroneous
- implicit criteria based on expert judgement
- mix of explicit and implicit criteria

Table 10 shows three definitions of medication errors which are frequently referred to. The first one was proposed by the US based National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP), an independent body comprised of 25 national and international organisations including the American Society of Health System Pharmacists.[51] This definition has been adopted by the NPSA [15], but the NPSA uses the term **"patient safety incident involving medicines"** instead of medication error.

"A medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm, while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems including: prescribing; order communication; product labeling, packaging and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use". (http://www.nccmerp.org/aboutMedErrors.html accessed 18.10.2004 or http://www.npsa.nhs.uk/ accessed 15.08.2005)
"Any error in the process of prescribing, dispensing or administering a drug".[29;40]
"Errors occurring at any stage in the process of delivering a medication whether there are adverse consequences or not."[52]
"The failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim"[53] (This is the definition of a human error, but has also been used as a definition of a medication error[54])

Table 10: General definitions of medication errors

The first three definitions listed in Table 10 emphasise that medication errors are related to the process of providing medication and (partly) stress that errors do not necessarily have to be associated with adverse patient consequences (in contrast to adverse drug reactions and adverse drug events). The first definition in Table 10 by the NCC MERP gives some characteristics of errors (preventable events of inappropriate medication use) and describes the circumstances where this medication use occurs. However, none of these definitions give any details of what is considered erroneous, thus all of them are based on implicit criteria. Terms such as 'preventable event' and 'inappropriate medication use' are very broad (what is more, error is equated with inappropriateness – most would think these concepts different). Subjective judgment is required to distinguish between what is correct and what is an error. This relies heavily on the knowledge, views and attitudes of the individuals that

judge the process and others may view the situation differently. Furthermore, in a lot of cases inappropriate medication use is not equivalent to a medication error. In summary, the first three definitions are circular, defining the 'medication' part rather than error.

The last definition listed in Table 10 is the description of errors originating in human error theory,[23] which is adapted by the Institute of Medicine in the US as their definition of medical errors.[53] A recent study quoted this as their definition of a medication error.[54] However, it depends on what the 'aim' is. Much of the psychology of human error literature comes from studying workers in industrial settings. They often had a single aim. In medicine the 'aim' may be a contestable balance of different ends, such as respecting autonomy while protecting the public good.

The definitions reviewed so far provide a general idea or description of medication errors, they do not provide sufficient detail to be used operationally to determine medication error rates. Even studies referring to the same definition are not necessarily comparable. Interpreting the results of studies using these broad definitions based on implicit criteria require careful review of the data collection methods and results to identify what was considered erroneous. This also highlights that the same act may or may not be judged an error depending on the circumstances, judges, healthcare system and culture. But there could be also an advantage of using an implicit definition of a medication error: processes of a diverse nature could be included which would be missed using explicit criteria.[55]

To obtain more detailed guidance about medication errors there is a need to focus on specific groups of errors such as prescribing errors and administration errors. In the following section we outline common definitions for these specific types of error.

Prescribing errors
Table 11 shows three commonly used definitions of prescribing errors. The first definition is one of the few examples of a definition which was based on a consensus method, suggested by Dean et al. [56] This was consequently used in a number of studies identifying the prescribing error rates as well as their causes.[24;30;57-60] Furthermore, it has been adopted in the report of the Department of Health "Building a safer NHS for patients – improving medication safety".[15]

The definition by Dean et al. (first one in Table 11) provides information about the characteristics of an error: it is unintentional and needs to be of clinical significance. Furthermore, this definition sets as its reference point generally accepted practice. In the original paper Dean et al. [56] also include examples to illustrate what is included and excluded as a prescribing error.

"A clinically meaningful prescribing error was defined as a prescribing decision or prescription writing process that results in an unintentional, significant reduction in the probability of treatment being timely and effective or increase in the risk of harm, when compared with generally accepted practice. Prescribing without taking into account the patient's clinical status, failure to communicate essential information, and transcription errors were all considered prescribing errors. However, failures to adhere to standards such as national guidelines or the drug's product license were not considered errors if this reflected accepted practice."[56]
"Prescribing errors were defined as errors in the name, strength or dosage form of a drug, in the dosage, in the route of administration, in the instructions for use, in the length or therapy or in the combination with the other medication used by the patient. […] Wrong indication was not included in the prescribing errors. […] A dosage was only considered to be too high when it exceeded the maximum dosage for all indications."[61]
"An error was determined to have occurred when an order was found to be incomplete, incorrect, or inappropriate at the time of physician ordering."[62]

Table 11: Definitions of prescribing errors

Another definition for prescribing errors was used in a study by van den Bemt et al.[61] (second definition in Table 11) This definition is circular – it defines "errors" as "errors" in the first six words. All it does is describe the scope of prescribing. Even the attempt to define an explicit standard for dosing errors is unclear – what does maximum dose refer to? The licensed dose – which can often be validly exceeded in practice? For example, it is accepted practice to prescribe doses of gentamicin which exceed the licensed dose for all indications. The last definition in Table 11 is also vague and ambiguous. What is the difference between an incorrect and an inappropriate prescription? The authors provide some more details about medication errors, but these are only partly helpful, for example "a wrong drug" is defined as an "incorrect drug ordered".[62]

Finally there are many studies of prescribing errors that do not give explicit definitions, but which investigate the incidence of "inappropriate prescribing" or medication errors as judged by reviewing pharmacists and prescribing physicians.[31;63-65] Whilst this is a pragmatic approach, again it is subjective and is likely to lead to wide variation.

Administration errors

Table 12 shows common definitions of administration errors. A definition which has been widely used to describe administration errors in hospital is the first one in Table 12: This was also the standard definition of a *medication error* adopted by the American Society of Hospital Pharmacists.[66] This is confusing, as this definition of a "medication error" specifically addresses medication administration errors. Obviously, this group of researchers refer to medication administration errors as medication errors.[67] Possibly this is because a lot of the early studies carried out by pharmacists in the United States, in particular by Barker and colleagues,[45] focused on medication administration errors.

"A medication error is a deviation from the prescriber's handwritten or typed medication order or from the order that the prescriber had entered into the computer system." [67]
"A deviation in preparation and administration of a drug from a doctor's prescription, the hospital's intravenous policy, or the manufacturer's instructions. The clinical appropriateness of the prescription was not assessed. All errors had to have the potential to adversely affect the patient, so deviations from hospital procedures, such as not checking name bands or not labeling infusions, were not considered as errors if the correct drug was given to the patient".[25]

Table 12: Definitions of administration errors

Similar definitions have been used to identify medication errors associated with the preparation and administration of intravenous medication in hospitals (second definition in Table 12).

Both definitions of administration errors outline a clear standard (for example a doctor's prescription) which is used to identify what is wrong. But even using these definitions the methods sections of papers have to be read carefully for further detail of what was included and excluded, for example whether deviations from prescribed

time of administration, or not shaking a bottle of liquid medication, were considered as a source of error. But we also find numerous studies that do not include sufficient details to understand which types of errors were studied.[54;68;69]

Furthermore, whilst the definition for intravenous drug administration errors [25] states that errors had to have the potential to adversely affect the patient, other studies also included deviations from processes which do not directly affect patient safety. For example, a study on intravenous drug errors included cases where nurses did not wear protective gloves when preparing antibiotics. However, this is recommended to prevent staff from developing allergies against the antibiotics.[37] Therefore, deviating from the standard would not affect patient safety.

3.3 Redefining the term "medication error" in practice

So far we have found a wide range of different definitions of medication errors in policy documents and research, but there are several studies showing an even greater variation in how the term medication error is defined and understood in practice. Ethnographic research investigated the criteria nurses used to decide whether an incident was a "real" error and consequently had to be reported through the medication error reporting scheme operated in the hospital.[70] For example, nurses did not regard incidents as medication errors if they were not their "fault". This included cases in which a drug was not administered, because it was not available on the ward or the patient was absent from his or her room which would be an omission error according to most definitions quoted above. Similar "redefining" strategies were found in a study interviewing hospital pharmacists.[71] For example, if prescribing errors were detected by the pharmacists and resolved in the pharmacy department they were named "interventions" and not reported via the medication error reporting system. Interviews with doctors about their prescribing errors also suggested that such incidents were not always interpreted as errors.[24]

Our review so far has shown that there is no generally agreed definition of a medication error. Most definitions are based on implicit criteria which are open to wide interpretation. This makes it difficult to compare study results.

3.4 Definitions describing harmful events and the role of medicines in its cause
Adverse drug reaction
Commonly used definitions for adverse drug reactions are listed in Table 13. The most widely used definition of an adverse drug reaction is that of the World Health

Organisation (WHO) which was originally published in 1972 [72] and with a slight modification is still in use.[73;74]

Comments in the WHO documents emphasise that this definition includes all doses prescribed clinically, but is intended to exclude accidental or deliberate overdose. There is no further reference made to differentiate adverse drug reactions from medication errors.

However, there is diversity in how the WHO definition is understood in this respect. Some studies and meta-analyses on adverse drug reactions (explicitly referencing the WHO definition) have included data on medication errors.[75-77] The NPSA also included adverse drug reactions as one type of "patient safety incident involving medicine" (i.e., medication error) as can be seen from the National Reporting and Learning System.[78] In contrast other authors conducting similar studies excluded data on medication errors, explicitly stating that adverse drug reactions were not due to medication errors.[52;79;80] Irey [81] mixed events that were adverse drug reactions as defined by the WHO with events which would not fall within the WHO definition, for example 'lethal adverse drug reactions involving diagnostic or therapeutic error'. Other authors have used their own terminology. The Boston Collaborative Drug Surveillance Program of Boston University defined adverse reactions as "undesired or unintended effect of a drug" including "deliberate or accidental overdosage and reactions to illicit drug use".[82;83] A recent document by the World Health Organisation [73] also suggests that pharmacovigilance centres, traditionally focused on collecting and analysing reports of adverse reactions to drugs, include reports of adverse reactions due to overdoses and medication errors. Medication errors are also addressed in publications of pharmacovigilance centres.[84-87] Interestingly, the recent report issued by the Chief Pharmaceutical Officer in the UK suggests that harmful medication errors were considered to be adverse drug reactions.[15]

Recently Edwards and Aronson [88] suggested a modified definition of an adverse drug reaction which is intended to include reactions due to medication errors (second definition in Table 13). Furthermore, they emphasised that reactions due to contaminants (e.g., in herbal medicines) also needed to be considered. Finally, they found the term "noxious" too vague and not suitable to differentiate sufficiently between very minor and harmful reactions.

"An adverse reaction to a drug is one that is noxious, is unintended, and occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function."[72]
"An appreciably harmful or unpleasant reaction, resulting from an intervention related to the use of a medicinal product, which predicts hazard from future administration and warrants prevention or specific treatment, or alteration of the dosage regimen, or withdrawal of the product."[88]
"An adverse drug reaction (ADR) is an unwanted or harmful reaction experienced following the administration of a drug or combination of drugs and is suspected to be related to the drug. The reaction may be a known side effect of the drug or it may be a new previously unrecognised ADR." (http://medicines.mhra.gov.uk/ourwork/monitorsafequalmed/yellowcard/whattoreport.htm accessed 15.8.2005)

Table 13: Definitions of adverse drug reactions

Although the authors intend to include medication errors, this definition would suggest that only certain types of medication errors are included. It excludes medication errors which did not cause harmful reactions as well as errors which involve the absence of a drug, such as omissions or underdosing.

A very similar definition to the ones already presented is the current definition of an adverse drug reaction used by the UK Medicines and Healthcare products Regulatory Agency (MHRA) (third definition in Table 13). There is no comment available that would suggest whether or not medication errors are considered to be included as a source of adverse drug reactions – the definition could be read in either way at present. As has been already highlighted, some of the documents that are published by the MHRA would suggest that they also receive reports of medication errors.

The above reviewed definitions of adverse drug reactions suggest that there is a shift in the area of pharmacovigilance to extend the "traditional" definition of an adverse drug reaction and include (certain types of) medication errors as a source of adverse drug reaction. This refinement in the understandings of pharmacovigilance needs to

be reviewed as it is bringing together different traditions of thought, something difficult to achieve well.

3.5 Difference and overlap between medication errors and adverse drug reactions

Whether or not medication errors are regarded as a source of adverse drug reactions, in practice it is sometimes difficult to classify an event clearly as one or the other. Therefore we have left an area of overlap between the two in Figure 29. We would like to illustrate this using the example of a patient who experienced allergic shock after the administration of penicillin. If this patient was known to be allergic to penicillin, it would be a medication error as this drug should have not been prescribed for the patient. If it was not known, it would be an adverse drug reaction. But in practice, it may not always be as easy to decide whether or not an error had occurred (Did the doctor forget to ask the patient about the allergy? Did someone forget to document the allergy in the patient's notes? Did the prescriber not check the notes? etc).

Apart from such practical issues of knowing whether or not an error had occurred we can also hypothesise that some events which are classified as adverse drug reactions today, may become medication errors in the future. For example, pharmacogenetic testing can be used to predict to what extent a patient metabolises certain drugs (e.g. distinguishes between slow, normal and fast metabolisers). This information can then be used to find the most suitable dose for this patient and prevent adverse reactions due to slow metabolisers being given a normal dose, which for them is an overdose. However, such techniques are not yet standard practice therefore not individualising the dosing regimen in this way cannot be regarded as an error.

Using these examples, the main difference between adverse drug reactions and medication errors is the extent to which such reactions can be prevented. As the second example on pharmacogenetic technologies suggests, preventability depends on the standard of care that is available and possible.

Related terms

The term adverse drug reaction is well established today,[89;90] but a review of papers and books published in the 1960s and 1970s shows that a range of other terms have also been used. For example, one of the pioneers of pharmacovigilance, the

physician L. Meyler, referred to "side effects". He established the series "Side effects of drugs" which continues to be published today. Reviewing the editorials of early editions of the series shows that other terms that were considered at the time include "untoward side effect",[91] "hypersensitivity to drugs" and "unwanted effects of drugs".[92]

Finally, many authors do not provide a clear definition of what exactly they studied. For example Caranasos and colleagues [93;94] published two studies on drug related events which used terms such as "drug-induced illnesses" and "adverse drug reactions" without providing a clear definition. They included adverse drug reactions (as defined by WHO) as well as events that seemed to have been due to errors.

3.6 Adverse drug event

The definition of an adverse drug event that is widely referred to is the one by Bates and colleagues of the Adverse Drug Event Prevention Study Group[40]. Studies carried out by Bates and colleagues identified harmful events that were possibly associated with drug use. Cases in which a causal relationship between drug use and harmful event could be established were called adverse drug events. The following definition was used:

"an injury resulting from medical intervention related to a drug" [40]

or

"injuries that result from the use of a drug".[29]

Adverse drug events are then further classified. In one of the group's first studies they classified the incidents into adverse drug reactions (WHO definition) and other incidents.[80] Later studies from the same group differentiated between non-preventable adverse drug events which are adverse drug reactions and preventable adverse drug events which are due to medication errors (for example in studies [29;40;47]). Thus preventable adverse drug events are medication errors which actually resulted in patient harm (excluding harmless errors). In some studies Bates and colleagues also include the category of potential adverse drug events. These are medication errors with the potential to harm the patient, but in this particular case no harm occurred (either due to lucky circumstances or because the error was prevented before reaching the patient). [29;40;47] Other studies refer to such events as "near misses". In recent studies by the same group the term ameliorable adverse

drug event is also used. These are events which are not preventable, but whose severity or duration could have been substantially reduced had different actions been taken.[95]

In summary, medication errors as defined by Bates' group have two main characteristics; they are harmful and they are preventable. Both of these characteristics are determined by subjective judgement. The level of harm they included is not defined, but remains the subjective judgement of the investigators. In contrast, a study which identified adverse events in medicine (including adverse drug events) defined harm as "measurable disability at discharge or increased length of stay due to the event".[96]

There are numerous other studies which adopt the usage of these definitions of adverse drug events established by Bates and colleagues.[97-100] But again, methods and results sections have to be carefully reviewed to identify what events were studied. For example, Classen and colleagues also use the term adverse drug event in their studies, but they define adverse drug events using the WHO definition of an adverse drug reaction.[101;102] However, careful review of their data suggest that they included incidents that were adverse drug reactions (as defined by WHO) as well as harmful medication errors.

The US Food and Drug Administration (FDA) uses the term adverse drug event for their spontaneous post-marketing surveillance system.[103] However, the aim of this program is to gain information about adverse drug reactions, but not medication errors. For example, on their website health care professionals can choose whether to report "adverse events" or "medication errors". For the latter they are then redirected to another website (http://www.fda.gov/medwatch/report/hcp.htm).

3.7 Adverse event

The term adverse event is mainly used in the context of clinical trials (pre- and post-marketing). According to the guidelines of good clinical practice, all adverse events that occur to patients during a clinical trial have to be recorded. The main feature is that there does not have to be a causal relationship between drug and the incident, which is in contrast to adverse drug reactions, adverse drug events and medication errors.

Adverse events are defined by the World Health Organisation as:

"any untoward medical occurrence that may present during treatment with a medicine but which does not necessarily have a causal relationship with this treatment".

This is very similar to the definition issued by the European Agency for the Evaluation of Medicinal Products as an international standard on clinical safety data management for reporting of drug-related incidents pre- and post-marketing.[89;90]

"Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment."

The term adverse event is also sometimes used for reports that are submitted to pharmacovigilance centres before formally assessing the likelihood of a causal relationship between event and drug exposure.[74;103]

Unfortunately, the terms adverse event and adverse drug event sound very similar and therefore in practice (and in publications) they may be mixed up or used as synonyms, although as shown above their meanings are quite different.

3.8 Near miss incidents

Another term which is often used in the context of medication errors or adverse drug events is "near miss incidents" or "close calls". There is also a range of definitions and descriptions for these terms and most of these do not refer specifically to medication errors, but to other adverse events in medicine and elsewhere. Mainly these are used in the context of error/adverse event reporting systems (Table 14).

In summary, the definitions suggest that near misses include errors which did not reach the patient, but had potential to harm the patient. The level of harm required to differentiate between a "near miss" and a "real error" is not specified. Likewise, it is not always clear whether medication errors which do not have the potential to cause harm to patients, for example the erroneous administration of two vitamin tablets instead of one, would be also called a near miss. The definition of the UK Department of Health suggests that such cases are included as a near miss.

Near miss: UK Department of Health, "Building a safer NHS - improving medication safety":[15] "Medication errors that do not result in patient harm or errors with the potential for harm but detected before they reach the patient" [104]
Near miss: UK Department of Health, "An organisation with a memory":[105] "A situation in which an event or omission, or a sequence of events or omissions, arising during clinical care fails to develop further, whether or not as the result of compensating action, thus preventing injury to a patient" [105]
Near miss: Institute of Medicine in the USA "Achieving a new standard for care":[106] "An error of commission or omission that could have harmed the patient, but serious harm did not occur as a result of chance (e.g., the patient received a contraindicated drug but did not experience an adverse drug reaction), prevention (e.g., a potentially lethal overdose was prescribed, but a nurse identified the error before administering the medication), or mitigation (e.g., a lethal drug overdose was administered but discovered early and countered with an antidote)" [106].
Close call: "Close call – is an event or situation that could have resulted in an adverse event but did not, either by chance or through timely intervention." [107]

Table 14: Definitions of a 'near miss' or 'close call'

3.9 Summary

This review shows the diversity of definitions to describe risks associated with medication use. Definitions are interpreted and used differently and contradictory use was identified. The following issues were identified:

- A broad range of definitions are used for medication errors and few definitions provide clear information about what is considered erroneous (explicit criteria), relying on subjective judgment (implicit criteria)
- Standards of care have an impact on the definition of a medication error and changing standards may change the definition of what is considered erroneous
- There is no agreement regarding whether or not "adverse drug reactions" may include causation by medication errors

- Most authors use the term adverse drug event to describe all types of medication related harm, but others use the term adverse drug event as a synonym for adverse drug reaction (excluding medication errors)
- Adverse drug event is the term that is used to encompass all harmful events that occur to patients whilst they take medication, but there is no clear definition of what degree of harm is considered harmful
- Some studies do not provide sufficient detail about the definitions used to measure drug related harm/risks

We recognise that the two different schools of thought (pharmacovigilance and medication error research community) approach the topic of drug safety from two different perspectives (individual drugs versus system of drug use). There is an overlap in interest of researching certain types of risks of drugs. This may be fruitful, but contains the risk of causing friction, because of different research traditions, methods and last but not least also terminology in understanding each other.

4. A review of commonly used methods to determine medication error rates

This section is based on the paper by Franklin et al. [50], due to be published in Drug Safety in 2005 (we are awaiting copyright permission to include parts of the article in this section). We include it here so the Chapter gives a rounded view of the variability that results from definitions and methods.

Many different methodologies are available for studying errors and adverse events, and each has its respective strengths and limitations.[108] In the following section we outline the main approaches used to identify medication error rates and highlight the strengths and limitations of these methods.

Studies of medication errors may be classified according to whether they focus on outcome or process, and whether study designs are retrospective or prospective (Table 15). We now consider each of these in turn.

	Prospective	**Retrospective**
Outcome based	Daily review of patient medical notes and asking staff for potential reports of harm [40]	Retrospective review of medical notes [109] or death certificates [110]
Process based	Pharmacist review of medication orders during prescription monitoring [111] Self reporting [48] Observation of drug administration [25]	Retrospective review of medication orders [112]

Table 15: Different types of medication error studies, with an example of a study of each type.

4.1 Outcome-based studies

Such studies are based on identifying actual patient harm. Most studies that fall into this category have included many different kinds of iatrogenic injury as well as medication errors. However, depending how the data are presented, the frequency of medication error-related events can sometimes be determined. Data collection can be either retrospective or prospective.

Retrospective studies of outcome

The Harvard Medical Practice study [96] is probably the most well known retrospective study of iatrogenic harm; this US-based medical notes based review suggested that adverse drug events occurred in 0.7% of inpatients. A more recent US study [113] suggests a similar figure of 0.6%. However, these figures include adverse drug reactions, as well as medication errors, and the published results do not allow differentiation between them. From a UK study using similar methodology,[114] it can be estimated that preventable medication-related harm (ie harm due to medication errors) occurred in 0.8% of admissions. However, some doubts have been cast over the validity and reliability of the assessment of preventability in such studies.[115] Furthermore, since the medical notes used as a data source were originally created for a different purpose, inadequacies in documentation could result in both false negative and false positive results.

Another approach to retrospective data collection is to use "triggers" such as the results of laboratory tests or medication prescribed that may indicate that an error has occurred. Data collection may be manual [116;117] or computerised.[118] However, the studies carried out to date focus on adverse drug events in general, and the results are not sufficiently detailed to allow differentiation between prescribing errors, other types of medication error, and adverse drug reactions. Furthermore, this methodology has not been fully validated and the percentage of all events that can be identified using this method is not yet known. When the real number of errors is low, it is easy for tests with low sensitivity and specificity to generate more false than true alerts.[119]

Few studies have reviewed death certificates to identify the medication error related death rate [120] or drug related death rate.[121] These studies depend on correct identification and documentation of medication related deaths and are therefore likely to be an underestimate. But they are a powerful reminder that medication errors can cause death and provide valuable information about high risk medication.

Prospective studies of outcome

Prospective approaches potentially offer a more rigorous and robust approach without some of the biases associated with retrospective review. Prospective studies allow additional checking and investigation that is not possible in retrospective reviews that may be carried out months or years later.

The US-based Adverse Drug Event (ADE) Prevention Study Group carried out a prospective study to examine medication-related harm in more detail.[40] ADEs included all types of medication errors that resulted in harm, as well as adverse drug reactions; ADEs were identified using self-reporting by practitioners and daily medical record review by researchers. It was concluded that medication errors caused harm in 1.8% of inpatients, of which prescribing accounted for the majority (1.0% of all inpatients). This approach is likely to be more comprehensive than retrospective methods; however, there are no studies that directly compare the two. As has been highlighted, definitions of harm also vary. For example, in the Harvard Medical Practice study,[96] harm was defined as "measurable disability at discharge or increased length of stay due to the event". This study therefore included only events that resulted in more serious levels of harm. The ADE Prevention Study Group did not define the level of harm they included, but suggest that "all" ADEs were studied; only 8% of the ADEs they identified met the definition used in the Harvard study.[40]

Computer-based [40;122-124] systems have also been developed to prospectively screen for ADEs, including preventable ADEs (medication errors), using similar triggers to those used in the retrospective methods described above. Prospective screening means that preventative action can be taken. However, in general, the results of published studies are not sufficiently detailed to report the medication error rates.

In outcome-based studies, only those errors that reach the patient and result in injury are included. The advantage of this approach is that only the errors that actually cause harm are included, removing the need to estimate the potential clinical significance of an event. However, the disadvantage is that errors that do not result in harm, either due to the intervention of another health care professional or due to sheer good fortune, are not included. This means that these errors cannot be learnt from. This is in contrast to the next type of study, those based on the process of prescribing and administering medication to the patient. The majority of studies in this field generally focus on one type of error, either prescribing or administration errors.

4.2 Process-based studies: Prescribing errors

These studies are based on health care professionals, usually pharmacists, reviewing prescriptions to identify prescribing errors. While such studies may be retrospective or prospective in design, the majority are prospective. Since pharmacists prospectively identifying prescribing errors will generally draw these to

the prescriber's attention, the prescriber will often correct the medication order before the patient receives any medication, or before many doses have been received. There are therefore few actual adverse outcomes. The majority of studies have been carried out in secondary care.

Retrospective studies of process
Twenty-five years ago, Tesh et al.[112] carried out a retrospective review of drug charts and medical notes in three wards in a UK hospital. It was concluded that 3.6% of all medication orders were associated with an error in drug use; these included errors in dose and frequency, route of administration and potential drug interactions. In addition, there were errors in prescription writing (such as use of brand names and spelling errors) in 7.9% of the medication orders studied. However, the definitions used are very broad, including prescribing by brand name, and the results cannot easily be compared with more recent studies.

Prospective studies of process
Studies show that US pharmacists prospectively reviewing medication orders in the course of their prescription monitoring duties identify (and prevent) prescribing errors in 0.3 to 1.9% of all orders written.[63-65;111] However, careful examination of these studies reveals some variation in the definitions used and comparisons amongst them should be made with caution. As one of the most prolific authors in this area points out, some of the error rates quoted are also likely to be an underestimate of the true error rate, as many errors will go undetected by the dispensary-based pharmacists who collected the majority of these data.[63] A study in paediatric inpatients used similar data collection methods to those used by the ADE Prevention Study Group, but included all medication errors instead of only those that resulted in harm.[29] In this study, a prescribing error was identified in 40.5% of admissions, or 4.2% of medication orders written.

There have been fewer studies outside of the United States. Several prospective UK studies have studied pharmacists' clinical interventions.[125;126] However, such studies do not allow firm conclusions to be drawn regarding the frequency of prescribing errors, as pharmacists' interventions may be for many other reasons, such as advice giving, formulary issues and patient counselling.

In a more recent study, pharmacists prospectively identified prescribing errors in UK hospital inpatients [30] using a standard definition of a prescribing error.[56] This study

identified a prescribing error in 1.5% of all medication orders written, and a potentially serious prescribing error in 0.4%.[30] All of these were identified by pharmacists during routine monitoring and were rectified.

In another UK study, Haw and Stubbs [58] examined prescribing errors in a psychiatric hospital and concluded that an error occurred in 2.2% of all prescription items checked. This denominator is different to the number of medication orders written, which is the denominator used in other studies; results are therefore not directly comparable.

Sagripanti et al.[57] studied prescribing errors in a cohort of 76 elective surgery patients who were followed from pre-operative assessment clinic to discharge in a UK hospital. Prescribing errors were found in 36% of medication orders written on admission, in 3% written during the inpatient stay, and 27% written at discharge. The latter were generally the omission from the electronic discharge prescription of medication that patients reported having supplies of at home. Other studies focus specifically on the admission process, with studies suggesting that unintentional discrepancies in medication history taking occur in up to 65% of all patients.[127]

4.3 Process-based studies: Administration errors

The majority of research to identify administration errors are prospective studies based on observation of nurses during the administration process. Administration errors are in general defined as deviations of administered medication from prescribed medication. These are identified by an observer, often a pharmacist, recording details of administered medication and comparing this with the original prescription of the physician. Barker and colleagues have been one of the first groups to use this method extensively in various studies in the US beginning in the 1960s.[128]

A review of UK studies showed that medication administration error rates associated with oral medication on general wards range between 3% and 8%.[129] Most of these studies excluded intravenous drug errors. Recent studies reported errors rates between13% and 84% observing preparation and administration of intravenous drugs.[25;37;130-132] Studies which focussed on administration errors in intensive care observed similar high error rates.[36;38] As observers often prevent serious errors from reaching the patient, little is known about the actual outcome of errors. Relatively few studies have used methods to assess the potential outcome of the errors.[33;35;133]

Studies focussing on oral drugs or medication administered in intensive care found few administration errors had the potential to harm the patient,[32;36;134] whereas, 1-3% of administered intravenous doses were associated with a potentially serious harmful error.[25;34] It has often been suggested that the presence of the observer may change the behaviour of the observed. But several studies have assessed the reliability and validity of the observation methods and found that the presence of the observer seems to have little impact on the error rate.[45;135] In addition, human error theory suggest that in most categories of error the person would not know they were making an error and hence could not alter their behaviour. However, it remains likely that error rates reported using this method will be a conservative estimate.

In one study, dosing errors were identified by analysing the concentration of intravenous infusions of acetylcysteine.[136] Errors were due to calculation mistakes, major errors in drawing up the drug and inadequate mixing of infusions. But such methods are difficult to use across a wide range of different drugs, are restricted to intravenous medication and some types of errors, such as the omission of prescribed medication are less likely to be detected. Other methods such as chart review and incident reporting were found to be unsuitable to measure medication administration error rates.[137]

4.4 Other methods

Studies based on self reporting of errors [2;138;139] can also be classified as prospective and in general do not focus on a particular type of medication error. However, the extent and nature of what is reported is likely to vary widely depending on the nature of the reporting system, the organisational culture, how easy it is to report and other factors. Reporting systems can be used to highlight commonly reported problems, and serve an important function in raising awareness and enhancing safety. It is important to be aware that the data cannot be used to obtain quantitative estimates of error rates due to the gross under-reporting that is known to occur.[122;128;140;141]

4.5 Denominators

Studies differ in the denominators used to calculate the error rate. Denominators that have been used include hospital admissions,[109] patient days,[126] prescriptions or medication orders written,[30] number of medication orders checked by pharmacists,[58] number of observed drug administrations plus medication that was prescribed but then omitted,[25] number of medication administration interventions.[38] It has been

shown that for studies of medication administration errors, the denominator used can have a dramatic influence on the error rate calculated.[32]

4.6 Summary

A range of methods are used to study the frequency of medication errors. Key issues are whether studies should focus on process or on outcome and whether methods should be retrospective or prospective.

- Process-based studies potentially allow all errors to be identified giving scope for the identification of trends and learning opportunities, but may be criticized for focusing on many minor errors unlikely to have resulted in patient harm. Alternatively, process-based studies should include a measure of potential patient harm.
- Outcome-based studies are likely to identify areas with most patient harm
- Retrospective studies may miss errors, because of lack of documentation and lack of real time information on clinical status of the patient.
- Extreme caution is needed when comparing frequencies of medication error rates identified using different methods.
- More work is needed to explore the reliability and validity of the different research methods
- There is a lack of standard reporting methods in research papers

5. Severity of medication errors

Medication errors range from those with very serious consequences to those that have little or no impact on the patient. The main focus is on preventing the former and therefore methods are needed to differentiate between (potentially) harmful and harmless errors. In this section we review the literature on methods used to assess the (potential) outcome of medication errors and highlight their strengths and limitations.

Studies can be broadly divided into those that estimate the potential outcome (as actual patient harm remains unknown) and those that provide information on actual patient outcome. As we have already highlighted, in prospective process-based studies on prescribing or administration errors the researchers often prevent the medication errors reaching the patient and therefore data about the outcome of the patient may not be available (for example [25;30]).

5.1 Methods to estimate potential outcome

Methods that have been used to estimate potential outcome can be broadly divided into those based on subjective assessment and those based on proxy indicators.

Methods based on subjective assessment

Subjective assessment relies on one or more experts judging the likely outcome of the error identified. Studies vary in their choice of experts and the number of experts that are asked to judge the errors. Studies have used one,[38] two [30;37] or more experts [64;137] or an unknown number of experts.[31;63;111] Experts that have been asked to judge the medication errors include (clinical/hospital) pharmacists,[36;37;142] pharmacologists, [30] physicians [38;137] and nurses.[35;143] None of the studies included patients. Several studies used different health care professionals to assess the errors. For example, a physician and two pharmacists,[64] a clinical pharmacist and a pharmacologist.[30] Few studies provide some detail about what the experts should take into account when judging the cases. For example Allan et al.[137] stated that information on the patient's condition, the drug concerned and the frequency of the error should be considered.

Several studies provided estimates of agreement between two or more independent assessors. These ranged between good [144] moderate [145] and low inter-rater reliability.[40;95] Only few studies have formally validated this approach, that is determined how many experts and the type of health care professional needed to get

a valid and reliable estimate of potential patient outcome. For example, a study showed that for medication administration errors, the mean score of four health care professionals judging the potential clinical significance of an error on a scale between 0 (representing no harm) and 10 (representing death) gives a valid and reliable estimate of the potential clinical significance of the error.[33] Part of the validation process showed that the expert's judgement of potential severity was similar to the true outcome for a subset of medication errors with known outcome. The judges should preferably include one doctor, one pharmacist and one nurse. This method has consequently been validated for use in Germany [35] and has been used in several observation-based studies on medication administration errors in the UK and in Germany.[25;32;34]

Folli et al.[64] used a different approach giving details about the errors for each level of harm. For example, potentially lethal errors included cases "when the dose of a drug with a very low therapeutic index is too high (10 times the normal dose)". Unfortunately, no further detail is provided about the basis of this list and whether this was validated, for example using "real cases of adverse outcome".

Categories of potential outcome

The potential outcome has been categorised very differently. Table 16 gives an overview of the systems and categories that have been used. Other studies used categorisations that were developed to categorise actual patient outcome.[36]

It can be argued that judging the potential outcome of medication errors should take into account the extent of harm that may potentially occur as well as the probability of this harm occurring. This would require two dimensional measures.[33] However, none of the existing methods allow both of these dimensions to be expressed explicitly.

Authors	Categories	Examples of categories
Allan Flynn et al. [137]	2	Potentially clinically significant; not significant
Dean et al. [30]	2	Potentially serious; not serious
Dean et al. [33]	3	Severe; moderate; minor
Folli et al. [64]	4	Potentially fatal or severe; potentially serious; potentially significant; problem orders

Table 16: Systems to categorise potential outcome of medication errors

Methods based on proxy indicators

These methods typically consider objective measures such as the type of error or the type of drug involved, and attempt to relate these to the severity of the medication error. For example, one of the first studies on medication administration errors used as an indicator of severity the therapeutic classification of the drugs involved;[45] the same approach was subsequently adopted by Hynniman et al.[146] and Tisdale.[147] In these studies, therapeutic classifications of the American Hospital Formulary Service were reviewed to identify those containing drugs that were likely to be associated with serious effects if given incorrectly. Drugs in the serious category included those affecting the central nervous system, antibiotics and cardiovascular drugs. Drugs in the "not serious category" included gastrointestinal drugs, vitamins and vaccines. The validity of this method is limited by the many exceptions to the broad therapeutic classifications. For example, the intravenous administration of a vaccine (intended for intramuscular use) may have more serious consequences than the administration of a nifedipine capsule instead of a nifedipine slow release tablet. Other instruments were developed in the USA to standardise the level of disciplinary action taken against nurses involved in medication errors. They contain multiple items, the scores for which are summed to given an overall index of severity. For example, Tyndall and Carlson [148] included type of drug, type of medication error, route of administration, and patient's condition. Dean et al.[149] developed a scoring instrument which included items on the legal status of the drug, the therapeutic index, use outside the license, number of repetitions of the medication errors in one patient. This instrument is relatively quick and simple to use. In contrast to previous methods they extensively assessed the reliability and validity of this method. Although the method was found to be reliable and valid to differentiate between minor and significant outcome it was not suitable to differentiate adequately between moderate and severe cases of medication errors. Validity has not been assessed for other scales that are available in the literature and therefore it remains of concern whether methods based on proxy indicators are suitable as a true measure of potential outcome.

5.2 Categorisation of actual outcome

Prospective or retrospective outcome-based studies provide information about the consequences of medication errors for the patient. Different methods have been used to categorise the level of harm. Table 17 shows an overview of commonly used categorisation systems.

Authors	Categories	Examples of categories
31;63;111;150	2	Nonserious; serious
47;151	3	Significant; serious; fatal or life threatening
102	3	Mild; moderate; severe
78	4	Low, moderate, severe, death
133	9	See Table 18

Table 17: Different systems to categorise actual patient outcome of medication errors/adverse drug events

A classification referred to widely is that of the US National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP). It is used for their nationwide reporting system as well as by other reporting systems in the US (United States Pharmacopeia and Institute of Safe Medication Practices) and in other countries.[152;153] It defines nine categories with the anchors of "No error: Circumstances or events that have the capacity to cause error" and "An error occurred that may have contributed to or resulted in the patient's death" (Table 18). Harm is defined as temporary or permanent impairment of the physical, emotional, or psychological function or structure of the body and/or pain resulting there from requiring intervention. However, this classification system is misleading as it attempts to cover two aspects: *Did an error occur at all?* (category A versus all other categories) and *What are the consequences of the error?* (categories C - H).

Other classification systems shown in Table 17 use only two or three categories. A wide range of terms is used to describe the different levels of harm. It is difficult to compare across different studies as the same term may refer to different levels of harm. For example, "serious" includes life-threatening events in one study,[150] but not in others [40;47] which have a separate category of life-threatening events. Interestingly, the terms serious and severe have both been used for the most harmful category (Table 16, Table 17).

In most studies, the outcome of the errors are categorised subjectively by one or more expert. Hardly any study provides details about the difference between the different levels of harm. Some studies provide estimates to what degree experts agreed on classification of the events. For example, studies carried out by Bates and colleagues [29;40;47] usually use two experts to classify the outcome with good inter rater reliability. Other studies only use one individual or do not report any details on the categorisation process.[102] In such cases, the reliability of using these scales remains unknown.

NO ERROR
Category A: Circumstances or events that have the capacity to cause error

ERROR, NO HARM
Category B: An error occurred but the error did not reach the patient
(An "error of omission" does reach the patient.)
Category C: An error occurred that reached the patient, but did not cause patient harm
Category D: An error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm

ERROR, HARM
Category E: An error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention
Category F: An error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization
Category G: An error occurred that may have contributed to or resulted in permanent patient harm
Category H: An error occurred that required intervention necessary to sustain Life

ERROR, DEATH
Category I: An error occurred that may have contributed to or resulted in the patient's death.

Table 18: The NCC MERP categories for patient outcome [133]

5.3 Summary

- It is important to differentiate between minor and severe outcomes of medication errors. More research is needed to develop reliable and valid methods to estimate potential patient outcome in studies which do not provide actual outcome data.

- There is no agreement about how harm is defined

- Different scales are used to categorise patient outcome which limits comparisons between study results

6. Summary

In this Chapter, we have reviewed common definitions of medication errors and research methods to identify the frequency of medication errors and measure their severity. Our review shows:

- In medication error research there is a lack of generally agreed definitions for basic terms and widespread confusion and contradicting usage of terms and definitions
- Many research methods lack assessment of reliability and validity
- There is a poor standard of reporting of the details of methods and definitions in publications

This means that comparisons between studies can only be made with great caution and the generalisability of many research results outside the study's institution is very limited.

This has implications on the work which we presented in Chapter 0. We investigated currently available data to establish a Heinrich ratio for medication errors. The lack of standard definitions and available methods to assess the clinical impact of medication errors result in great uncertainty about the relationship between minor and more serious medication errors.

The findings of this Chapter also have wider implications for medication error research. There is an urgent need for the development of a common international system for defining, classifying, measuring and reporting adverse events and "near misses". The WHO has recently announced that it will initiate an international project on methods of intercountry comparisons to contribute to the development of a common international taxonomy in the area (http://www.who.int/patientsafety/en/).

A first step in these efforts would be to improve the reporting of results in medication errors research through a consensus statement. Such efforts were very successful in the area of improving the quality of conducting and reporting results of clinical trials, in which use of the CONSORT Statement is standard.[43] In the coming years many resources nationally and internationally will be dedicated to patient safety research. A consensus statement could improve research and reporting of research enormously and thus the generalisability of the results.