Bayesian Networks for Clinical Decision Making

Support, Assurance, Trust

Submitted in partial fulfilment of the requirements

of the Degree of Doctor of Philosophy

by

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Declaration

I, Evangelia Kyrimi, confirm that the research included within this thesis is my own work or that where it has been carried out in collaboration with, or supported by others, that this is duly acknowledged below and my contribution indicated. Previously published material is also acknowledged below.

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Date: 07/02/2019

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Abstract

Bayesian networks have been widely proposed to assist clinical decision making. Their popularity is due to their ability to combine different sources of information and reason under uncertainty, using sound probabilistic laws. Despite their benefit, there is still a gap between developing a Bayesian network that has a good predictive accuracy and having a model that makes a significant difference to clinical decision making.

This thesis tries to bridge that gap and proposes three novel contributions. The first contribution is a modelling approach that captures the progress of an acute condition and the dynamic way that clinicians gather information and take decisions in irregular stages of care. The proposed method shows how to design a model to generate predictions with the potential to support decision making in successive stages of care.

The second contribution is to show how counterfactual reasoning with a Bayesian network can be used as a healthcare governance tool to estimate the effect of treatment decisions other than those occurred. In addition, we extend counterfactual reasoning in situations where the targeted decision and its effect belong to different stages of the patient's care.

The third contribution is an explanation of the Bayesian network's reasoning. No model is going to be used if it is unclear how it reasons. Presenting an explanation, alongside a prediction, has the potential to increase the acceptability of the network. The proposed technique indicates which important evidence supports or contradicts the prediction and through which intermediate variables the information flows.

The above contributions are explored using two clinical case studies. A clinical case study on combat trauma care is used to investigate the first two contributions. The third contribution is explored using a Bayesian network developed by others to provide decision support

in treating acute traumatic coagulopathy in the emergency department. Both case studies are done in collaboration with the Royal London Hospital and the Royal Centre for Defence Medicine.

Contents

Glossary of Abbreviations

AI . . . . . Artificial Intelligence

AIS . . . . . Abbreviated Injury Scale

ADMEM . . . . . Academic Department of Military Emergency Medicine

ASCOT . . . . . A Severity Characterization Of Trauma

ATC . . . . . Acute Traumatic Coagulopathy

BN . . . . . Bayesian Networks

CDS . . . . . Clinical Decision Support

CI . . . . . Confidence Interval

CPT . . . . . Conditional Probability Table

CTBN . . . . . Continuous Time Bayesian Network

DBN . . . . . Dynamic Bayesian Network

DMS . . . . . Defence Medical Services

DOW . . . . . Died Of Wounds

ED . . . . . Emergency Department

EM . . . . . Expected Maximization

GCS . . . . . Glasgow Come Score

HTBN . . . . . Hybrid Time Bayesian Network

ICU . . . . . Intense Care Unit

ISS . . . . . Injury Severity Score

IT . . . . . Information Technology

ITBN . . . . . Irregular Time Bayesian Network

JTTR . . . . . Joint Theatre Trauma Registry

KIA . . . . . Killed In Action

KNEA . . . . . Killed Non Enemy Action

KL . . . . . Kullback Leibler

MACE . . . . . Major Trauma Audit for Clinical Effectiveness

MAR . . . . . Missing At Random

MB . . . . . Markov Blanket

MERT . . . . . Medical Emergency Response Team

MM . . . . . Max Mardsen

NHS . . . . . National Health Service

NISS . . . . . New Injury Severity Score

nsDBN . . . . . non-stationary Dynamic Bayesian Network

NT . . . . . Nigel Tai

RCDM . . . . . Royal Centre for Defence Medicine

RLH . . . . . Royal London Hospital

RR . . . . . Respiratory Rate

RTS . . . . . Revised Trauma Score

SM . . . . . Somayyeh Mossadegh

TNBN . . . . . Temporal Nodes Bayesian Network

TRISS . . . . . Trauma Injury Severity Score

TV-DBN . . . . . Time Varying Dynamic Bayesian Network

UK . . . . . United Kingdom

US . . . . . United States

WHO . . . . . World Health Organization

WIA . . . . . Wounded In Action

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Chapter 1

An Introduction to the Research Project and its Objectives

This chapter provides a thesis introduction and layout. Information on publications, paper submitted for publication and conference presentations, as a result of this research project, are presented.

1.1 Introduction

Clinical decision making is a complex evolving process, where evidence is gathered, and decisions are made [259]. Looking at the symptoms, patient's history and test results, clinicians try to answer two main question: 'What is the problem?' and 'How can we solve it?'. The countless symptoms, diagnostic tests, diseases, treatment options as well as the complex human physiology and the increased uncertainty, make clinical decision making a challenging task. Even though clinicians are good decision-makers, they often find it challenging to combine all the available evidence in their everyday clinical practice [73], [167], [96]. Wrong decisions are not uncommon, and they have been the source of public scrutiny [59]. Mistakes can happen for various reasons, such as human's biases, faulty heuristics, insufficient evidence, and incorrect or misused knowledge [263], [27].

Understanding clinical reasoning is important for supporting clinical decision making [204]. In early 50's, Lendley and Lusted were the first who tried to analyse the concept of medical reasoning. They focused mainly on explaining the complicated reasoning inherent in medical diagnosis, and on investigating ways to support that process [144]. Since then, many

researchers tried to understand how clinicians think and take decisions [72], [204], [8], and especially how they reason under time pressure [79], stress [123], and uncertainty [263], [135], [27], [262]. Clinicians very often rely on their intuition to take a decision [242], [79]. Intuition is not an abstract concept, but it represents the lessons learned and knowledge gained through many years of experience [183]. When clinicians face a problem that is familiar, they subconsciously select an action before a structured thought process is followed [50]. Intuition is quick and easy, and it can assist high quality decisions, especially for experienced clinicians [23], [183]. However, several drawbacks exist. First, intuition cannot be explained as there is no underlying reasoning but a 'gut feeling'. When such a decision is suboptimal, then there is no defence for choosing that decision. In addition, even for experienced clinicians, intuition can lead to several biases, such as neglect of the base rate, and heuristics, such as the availability heuristic that leads to a biased recall of the more vivid or recent cases [263]. Those biases and heuristics can also result in inconsistent treatment of similar cases [232]. On the other hand, how do clinicians take decisions when they are not experienced, or the case does not fit to any familiar pattern? In such cases, it is common to use rule-based methods, such as guidelines and procedural checklists [214]. This process can be easily explained but involves more mental effort than intuition [79]. In addition, there is not always a reasonable rule to describe a complex situation.

Lessons learned from studying clinical decision making and the important breakthroughs of statistics and Artificial Intelligence (AI) in medicine has led to the development of a more formal way to support decision making using clinical decision support (CDS) models [239], [61], [18], [205], [2], [45], [147]. These models are referred to by many names: clinical prediction rules, prediction models, decision rules etc. According to Wyatt and Spiegelhalter, a CDS model is defined as 'an active knowledge system which uses two or more items of patient data to generate case-specific advice' [275]. CDS models are mathematical tools that can integrate various sources of information and guide clinicians in their everyday decision making [116]. Many studies have shown that recommendations from a CDS model can be superior to clinicians' judgement [170], [22], [91], [76]. Unlike many clinicians, a CDS model can account simultaneously for multiple factors, like patient characteristics, symptoms, diagnostic test results to suggest a diagnosis or identify the most effective intervention [1], [148], [176], [95]. In contrast to intuition, a CDS model has an underlying reasoning process that gives consistent predictions for identical evidence. Finally, unlike

guidelines, a CDS model can offer a personalised support for each patient.

Many types of CDS models exist. These models have evolved from simple scoring systems to more complicated multivariate regression models, neural networks, decision trees, and probabilistic models [1], [90], [2]. Graphical probabilistic models, such as Bayesian Networks (BNs), have become a popular CDS model in medicine [155], [157]. The popularity of BNs in medical applications is due to their ability to combine different sources of information and reason under uncertainty, using sound probabilistic laws [208]. A BN is composed of a graphical structure that represents the relations between the variables, and a set of parameters that defines the strength of these relations. The graphical structure helps us to represent our knowledge about a disease, and its related symptoms, diagnostic tests and treatments. The strength of the relations among those factors can be learned from data and/or other sources of evidence such as published results and expert knowledge.

Many BNs have been developed in medicine [155], [157]. However, they are not always able to support clinical decision making [147], [24], [216], [261], [176], [174]. A BN can assist decisions taken at a specific time point. However, clinical decision making is an evolving process, as clinicians take several decisions during the patient's care. Several temporal extensions of BNs have been proposed to assist the dynamic nature of clinical decision making [181], [193], [223], [92], [202], [150]. However, there are still many challenges that need to be addressed when we model a medical condition that evolves rapidly over a short timescale and decisions are taken at irregular stages of the patient's care based on an increased amount of information.

We can assist clinical decision making not only by helping clinicians to take multiple decisions in successive stages of the patient's care, but also by re-evaluating those decisions after they are made. Useful lessons can be learned by reviewing already made decisions and investigating hypothetical scenarios [123]. These lessons can be used to improve future clinical decisions and assure optimal clinical practice [69]. Unlike other CDS models, BNs can compare the actual with the hypothetical world using counterfactual reasoning [243], [208]. Counterfactual reasoning with BNs has been used in medicine before, but never as a healthcare governance tool to estimate the effect of clinical decisions, such as treatment decisions, other than those occurred.

Finally, a CDS model is not going to be useful and used to assist clinical decision making if it is unclear how it reasons. A clinician is less likely to trust a model that he does not understand. We can understand something that it is explained to us using simple and familiar terms. As Aristotle wrote 'we do not have knowledge of a thing until we have grasped its why, that is to say, its explanation'. An explanation is a process of understanding a statement by providing causal connections to known facts [166]. In contrast to many CDS models, a BN is not a black box model and its reasoning can be explained [138]. Despite the existing approaches to explain the reasoning in BNs, a practical approach that gives a simple but sufficient explanation is still needed.

1.2 Research Objectives

As explained before, clinical decision making is the dynamic process of gathering evidence to take decisions that involve a high degree of uncertainty. Aiming to support clinicians' ability to deal with complex problems and take decisions, and not to replace them, many CDS models have been developed. Despite, the benefit of using BNs to assist clinical decision making, there is still a gap between developing a BN that has a good predictive accuracy and having a BN that makes a significant difference to clinical decision making. The main objective of this thesis is to bridge that gap. Three smaller, secondary objectives, related to (1) *Support*, (2) *Assurance*, and (3) *Trust*, helped us to achieve our main objective. The secondary objectives aim to:

1. Investigate how we develop CDS models that capture the progress of an acute condition and the dynamic way in which clinicians gather clinical information and take decisions with the potential to *support* clinical decision making in successive stages of the patient's care.

2. Investigate how we can use a CDS model as a healthcare governance tool to review and evaluate past treatment strategies with the potential to *assure* optimal future clinical decisions and clinical practice.

3. Investigate how we can make the reasoning of a CDS model clearer to clinicians to increase their *trust* in the model and the chances of using it.

The above objectives are explored using two clinical case studies. A clinical case study on combat trauma care is used to investigate the first two objectives. The aim of this case study is two-fold. Firstly, it provides a mortality risk prediction in irregular stages of the soldier's care, where many decisions are taken based on uncertain and limited information. Secondly, it is used as a healthcare governance tool to review whether the clinical practice was optimal and nothing more could have been done. The case study is done in collaboration with the trauma unit at the Royal London Hospital (RLH). Further collaboration was with the Academic Department of Military Surgery and Trauma within the Royal Centre for Defence Medicine (RCDM). The third objective is explored using a clinical BN developed by others in an earlier collaboration with the RLH and RCDM [282], [280]. This case study provided decision support in treating acute traumatic coagulopathy for injured civilians in the emergency department (ED). AgenaRisk software was used for building and training the BNs presented in this thesis [4].

1.3 Structure of the Thesis

In order to achieve our objective, this thesis is organised as follows:

Chapter 2 presents an introduction to Bayes theory, BNs and their conditional independence properties. The introduction is followed by a review of the reasoning process in BNs and a review of the time-based BNs that could be used to model the dynamic process of decision making. This background knowledge is necessary to follow the contributions introduced in Chapters 5, 6, and 7.

Chapter 3 explains the use of CDS models to assist decision making. It describes the barriers that the existing models may face when they are used in medicine, and investigates the reasons why some models are not as useful for practical decision support as might be hoped. The challenges described in this chapter are addressed in Chapters 5 and 7.

Chapter 4 introduces the combat trauma care case study. This chapter presents the challenges of building successful clinical decision support models for this domain. Those challenges are addressed in Chapters 5 and 6.

Chapter 5 proposes a method for building a CDS BN that captures the rapid progression

of an acute medical condition and the dynamic way clinicians gather information and take decisions in irregular stages of care. The proposed CDS BN provides a mortality risk prediction in successive stages of the patient's care with the potential to support clinical decision making. The methodology is illustrated by the combat trauma care case study.

Chapter 6 proposes a way of using counterfactual reasoning with BNs as a healthcare governance tool to estimate the effect of treatment decisions other than those occurred. Counterfactual reasoning with BNs is also applied in situations where the targeted decision and its effect belong to different stages of the patient's care. The review of combat deaths is used as a case study.

Chapter 7 proposes a technique for explaining BNs' reasoning. A comparative study to examine the effect of the explanation on clinicians' trust and decision making is also presented. A BN developed by others to provide decision support in treating acute traumatic coagulopathy for injured civilians in the ED is used a case study.

Chapter 8 summarises the progress made in Chapters 5, 6, and 7, and discusses the future directions of research.

1.4 Publications and Awards

The work in this thesis has led to the following list of publications, conference presentations and awards.

Publications

1. Kyrimi E, Marsh W. 'A Progressive Explanation of Inference in Hybrid Bayesian Networks for Supporting Clinical Decision Making', in the Eighth International Conference on Probabilistic Graphical Models, vol. 52, pp. 275-286, 2016. [137]

2. Kyrimi E, Mossadegh S, Mardsen M, Tai N, Marsh W. 'Counterfactual Reasoning with Bayesian Networks as a Healthcare Governance Tool', *In preparation*.

3. Kyrimi E, Mossadegh S, Mardsen M, Tai N, Marsh W. 'Modelling the Progress of an Acute Medical Condition to Support the Dynamic Nature of Clinical Decision Making', *In preparation*.

Conference Presentations

1. Kyrimi E, Marsh W. 'A Progressive Explanation of Inference in Hybrid Bayesian Networks for Supporting Clinical Decision Making', in the Eighth International Conference on Probabilistic Graphical Models, Lugano, Switzerland, 2016.

2. Kyrimi E, Mossadegh S., Marsh W., Tai N 'Counterfactual Reasoning with Bayesian Networks as a Healthcare Governance Tool to Enhance Defence Medical Services', in the Fourth International Conference on Operational Planning, Technological Innovations and Mathematical Applications, Hellenic Army, Athens, Greece, 2017.

Awards Our work 'A Progressive Explanation of Inference in Hybrid Bayesian Networks for Supporting Clinical Decision Making' presented as a poster in the Fourth Annual UK Causal Inference Meeting (London), received the best poster award. This work is explained in detail in Chapter 7.

Chapter 2

An Introduction to Bayesian Networks

This chapter introduces Bayes' theorem and BNs. Then, the properties of conditional independence and the types of reasoning in BNs are described. Finally, we review the existing methods for developing time-based BNs. The material included in this chapter is necessary to follow the novel contributions described in Chapters 5, 6, and 7.

2.1 Bayesian philosophy

The core of Bayesian philosophy is highly related to how we handle uncertainty. The simple idea upon which Bayesian philosophy is founded says that the only satisfactory description of uncertainty can be achieved through probabilities. Uncertainty is present in everyday life and Bayesian philosophy gives us the tools to quantify and control it [52], [77]

Bayesian philosophy considers the probability of uncertain events as a measure of a person's belief for this event. In other words, a probability is a subjective quantity that expresses one's willingness to bet on an uncertain event. This concept is different to the frequentist philosophy in which the unknown event is considered as random and not uncertain and its likelihood represents the frequency of observing the event in a fixed set of repeated experiments. There has been an endless debate between the two philosophies that is beyond the scope of this thesis [68], [264].

2.1.1 Bayes' Theorem

In late 1750, the English Mathematician Reverend Thomas Bayes developed the famous Bayes' theorem [17]. His study was focused on how to compute a distribution for the prob-

ability parameter of a binomial distribution and how prior beliefs can be updated based on new evidence; a process that we now call Bayesian inference, where initial beliefs are stated as prior probabilities and updated beliefs, in the light of new evidence, are stated as posterior probabilities.

Bayes' theorem is a simple equation which relates conditional and marginal probability distributions of variables and shows how a conditional probability depends on its inverse conditional probability. According to Bayes' theorem, the probability of a variable A conditioned on a variable B can be calculated as:

$$P(A|B) = \frac{P(B|A)P(A)}{P(B)} \tag{2.1}$$

If we consider the events $A_1, \ldots, A_k$ that partition the event space Ω, such as $A_i \cap A\,j = \emptyset\ \forall$ $i \neq j$ and $A_1 \cup \cdots \cup A_k = \Omega$, then Bayes' theorem can be extended:

$$P(A_i|B) = \frac{P(B|A_i)P(A_i)}{\sum_i P(B|A_i)P(A_i)} \tag{2.2}$$

The process of updating our prior belief about an event in the light of new evidence is common in our everyday life. In medicine for example doctors update their belief about a disease given some observed symptoms or the results of diagnostic tests. Suppose for instance that the prevalence of lung cancer in a particular community is 5.5%, and 11% of the people in the same community had a diagnostic test that confirms the presence of lung cancer (positive X-ray). Using the medical records of the community's hospital we know that 98% of the patients who had been diagnosed with lung cancer also had a positive X-ray. Now, we would like to know the likelihood of having a cancer given that one has a positive X-ray. Using Bayes' theorem, we have:

- The binary variable A : 'Does the patient have cancer?'
- The binary variable B : 'Does the patient have a positive X-ray?'

$$P(A = Yes|B = Yes) = \frac{P(B = Yes|A = Yes)P(A = Yes)}{P(B = Yes)} = \frac{0.98 \times 0.055}{0.11} = 0.49 \tag{2.3}$$

So the evidence of a positive X-ray increased the probability of having cancer from 5.5% to 49%. Bayes' theorem is easy to calculate when we have one hypothesis and one piece of evidence. However, it becomes rather complex when we have more hypothesis and

multiple pieces of evidence. In such cases, we prefer to use graphical probabilistic models, also known as belief networks or BNs. The following section introduces the basic features of BNs.

2.2 Bayesian Networks

BNs are built on Bayes' theorem and they provide a graphical framework for compact representation of multivariate probability distributions and efficient reasoning under uncertainty. Formally, a BN D is a pair $\{G, \Theta\}$, where G represents the graphical structure of the model and Θ is a set of parameters. More specifically, G is a directed acyclic graph in which nodes represent uncertain variables and edges denote probabilistic dependencies between connected variables. If a directed edge connects variables A and B, such as $A \rightarrow B$, then A is called parent node or ancestor of B and B is a child node or a predecessor of A. On the other hand, the set of parameters Θ specifies the strength of the dependencies between the variables in G, defined as conditional probability distributions.

Let $X = X_1, \ldots, X_n$ be a set of variables modelled in G, and let $\Theta = \{\theta_{X_i|PA_{X_i}}\}$ be the set of parameters that represent conditional probability distributions for each node X_i given its parents PA_{X_i}. The distributions $P(X_i|PA_{X_i})$, associated with each node X_i, are called local probability distributions [97]. BNs factor the joint probability distribution over X into a product of local distributions:

$$P(X_1, \ldots, X_n) = \prod_{i=1}^{n} P(X_i|PA_{X_i}) \tag{2.4}$$

Figure 2.1 shows a well-known medical BN called Asia BN which aims to diagnose the likelihood of 3 medical conditions; tuberculosis, lung cancer and bronchitis. Asia BN has 8 binary nodes and 8 edges. Each variable in Asia BN has a set of parameters that defines its probabilistic relation with its parents, presented by a conditional probability table (CPT). A CPT contains probability values for each state of the variable given every combination of the states of its parents. Table 2.1 shows the CPT of the variable 'Has Cancer?'.

BNs are not limited to work only with discrete nodes. Continuous nodes can be used as well. The probability distributions of continuous variables can be defined using statistical distributions. For more information on the theory of BNs and on how we model discrete

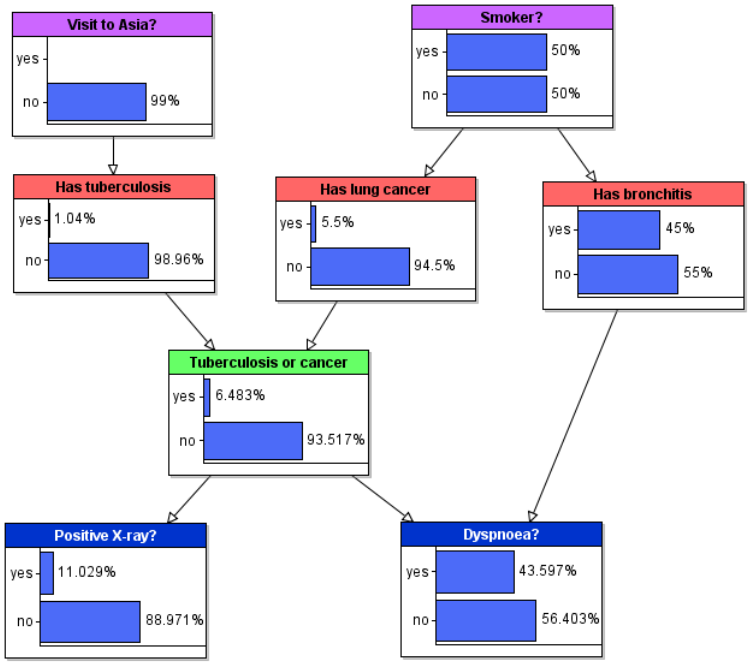

Figure 2.1: Asia BN

		Smoker?	
		Yes	No
Has Cancer?	Yes	0.1	0.01
	No	0.9	0.99

Table 2.1: CPT for the variable 'Has Cancer?'

and continuous variables in BNs see [250], [186], [111], [184], [185], [270], [127], [208], [74]. In the following section we give more insight into the stages of building a complex BN, focussing on knowledge engineering methods.

2.3 Building Complex Bayesian Networks

Building a BN comprises of two main components:

1. *Structure:* Determining the graphical structure involves identifying the variables that are important in the problem and should be included in the model, as well as defining the states of each variable. The last part of the structure is about the relations between the selected variables, and the direction of those relations.

2. *Parameters:* When the graphical structure is defined, the next step is to choose the parameters of each variable. The parameters represent the strength of the relations in

the BN structure.

Both BN structure and parameters can be built by automated learning from data, if enough data is available, 'by-hand' using elicitation methods to capture expert knowledge and to extract necessary information from the literature or by a combination of these. It is not always feasible or appropriate to use automated techniques and many times the structure and/or the parameters of the BN have been built by-hand. Large complex BNs are difficult to visualise and hard for the domain experts and the model experts to understand. Many knowledge engineering methods have been proposed over the years to facilitate the development of complex BNs. Some of the most well-known knowledge engineering methods are reviewed in the remainder of this section. Methods for developing complex BNs that are data driven or that are based both on data and experts are out of the scope of this section. A review of these methods can be found in [130], [280].

2.3.1 Knowledge Engineering Methods: Structure

It is nearly impossible to build a complex BN in one go. The most intuitive knowledge engineering approach to build a complex BN is to divide the problem into more tractable sub-problems. This is known as 'divide and conquer'. One way to achieve that is by dividing the model into clear sub-components, which become sub-networks in the BN.

Laskey and Mahoney recognised very early that BN construction requires a method for specifying semantically meaningful building blocks, they called network 'fragments' [142], [140]. A network fragment consists of a set of related random variables together with knowledge about their relations. Ideally fragments should make sense to the expert who must be able to supply some underlying motive or reason for them belonging together. Also, Mahoney and Laskey demonstrate the use of stubs to represent collections of BN nodes that have yet to be defined with the purpose of allowing early prototyping of partial BNs [162].

Another way to do incremental modelling is to vary the level of abstraction. There are two ways to achieve that: (1) using a top-down approach, where you see the problem at the highest level of abstraction first, and then you add increasingly more details at each of the pieces, and (2) the bottom-up approach, where the modelling starts at a detailed level. In practice, top-down and bottom-up modelling are usually combined. Koller and Pfeffer pro-

posed an abstract approach to support such modelling, known as object oriented Bayesian networks (OOBNs) [128]. OOBNs have become popular in building large BNs and many researchers have tried to improve their characteristics and facilitate their use [14], [230]. An OOBN is made up of classes that contain both ordinary nodes and objects, which are instances of other classes. A class can be considered as a network fragment. OOBN are particularly useful for complex models that contain repeated fragments, where objects can be reused to decrease the modelling effort.

In 2000 Neil et al. proposed a specific BN fragment, called an idiom [163]. An idiom is a natural and reusable reasoning pattern that can help to develop BNs efficiently and consistently. An idiom can be considered as a more cohesive entity than a fragment as it has associated semantics. Once probability values have been assigned to idioms then they become equivalent to objects in an OOBN and can be used accordingly.

Laskey and Mahoney propose a system engineering approach that uses a spiral lifecycle model for BN development [141]. A spiral model views the modelling as cycle, where the lessons learned at each stage are used to plan the next stage of the development [25], [130]. This approach starts by defining objectives and building initial prototypes with simple features. These prototypes are evaluated and rebuild. This process helps the model expert to understand the domain and the domain expert to understand the principles of BN modelling.

2.3.2 Knowledge Engineering Methods: Parameters

Eliciting parameters from experts can be time-consuming. Therefore, the first step is to reduce the size of the parameter space. The parameter space of a variable grows rapidly as the number of its parent variables increases. Adding an intermediate variable between the variable and its parents can reduce the size of the parameter space. This approach is known as 'parent divorcing' or 'synthesis idiom' [163].

Another way to facilitate parameter elicitation is using logic functions for binary nodes. Functions such as OR, AND or noisy OR gates decrease the number of parameters in a CPT by assuming that the effect of each parent variable is independent from other parents [101], [213], [283], [58], [208]. Parent divorcing and logic functions can be used together with parameter learning approaches when data is not large enough.

Fenton et al. proposed a simple approach for eliciting the parameters for ranked nodes [75]. The approach is based on the doubly truncated Normal distribution with a central tendency that is invariably a type of weighted function of the parent nodes. In this approach, parameters are defined by (1) selecting a suitable ranked node function for modelling the relation between the variable and its parents, (2) eliciting the weights of these relations from domain experts, (3) eliciting the expert's degree of confidence in these weights. A ranked node requires fewer parameters compared to a complete CPT, therefore the elicitation task requires significantly less effort. However, selecting a suitable function for the elicited relation can be challenging as it demands thorough understanding of the behaviour of different ranked node functions.

The parameters of a BN can be elicited from domain experts without using any data. The problems of bias and poor calibration that are typically encountered when eliciting judgemental probabilities from experts are widely known [263], [136]. Just as observational data and the methods used to collect them are subject to scrutiny, so should expert knowledge be scrutinized to ensure that uncertainty is quantified and bias in the elicited information is minimised [197]. The process of eliciting BN parameters from domain experts can be roughly divided into five stages [197], [134], [164], [196]: (1) select and motivate the experts, (2) structure the questions, (3) train the experts, (4) elicit experts' judgement and (5) verify the results. Many techniques for eliciting experts' judgement have been proposed. Most of them are simple and are based on scales with verbal and/or probabilistic anchors. Other methods use qualitative probabilistic networks or frequencies or even lotteries. More information about the existing approaches and their advantages and disadvantages can be found at [82], [220], [218], [219], [81], [198], [113].

2.4 Conditional Independence in Bayesian Networks

An important element in probability theory and BNs is the independence and conditional independence among variables. Using the law of probabilities, two variables A and B are independent ($A \perp B$) if $P(A,B) = P(A)P(B)$. Similarly using Bayes' theorem, $A \perp B$ if $P(A|B) = P(A)$. Two variables A and B can also be conditional independent given a third variable C if $P(A,B|C) = P(A|C)P(B|C)$. Conditional independences in BNs can be easily

computed using the concept of d-separation [206].

Suppose that we have three variables A, B and C and we want to know whether the variables A and B are d-separated given the variable C. There are three types of connection as shown in Figure 2.2:

- Serial connection (Figure 2.2a): A and B are d-separated given that the variable C is known.
- Diverging connection (Figure 2.2b): A and B are d-separated given that the variable C is known.
- Converging connection (Figure 2.2c): A and B are d-separated only if the variable C or any of its descendants are unknown.

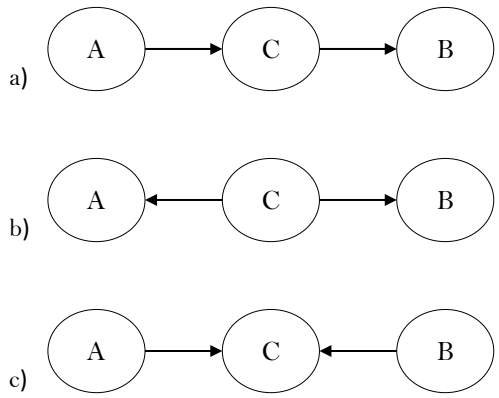

Figure 2.2: D-separation: (a) Serial connection (b) Diverging connection (c) Converging connection

When variables A and B are d-separated, then the information from variable A does not flow to variable B and vice-versa. In other words, d-separation affects the reasoning process. The next section gives an insight on the different types of reasoning with BNs.

2.5 Reasoning with Bayesian Networks

This section introduces three ways of reasoning with BNs; reasoning from observations, interventional reasoning and counterfactual reasoning.

2.5.1 Reasoning from Observations

Observations represent the real world, what actually happened. When we enter an observation, the BN uses this information to update the probabilities of the remaining variables. Reasoning from observations is the subject of probability theory and statistics and it can be derived from a joint distribution over the observed variables. Causal relationships are not necessary in this type of reasoning, as the focus is only on associative relationships. In observational reasoning, the information does not flow only from the parent to the child node, but it can also flow backwards from the child to the parent node. Using the Asia BN (Figure 2.1) we illustrate these two different directions of reasoning from observations:

1. Forward reasoning: In Figure 2.3a, knowing that the patient is a smoker increased the likelihood of having lung cancer (prior: 5.5%, posterior: 10%).

2. Backward reasoning: In Figure 2.3b, knowing that the patient's X-ray was positive increased the likelihood of having a lung cancer (prior: 5.5%, posterior: 49%).

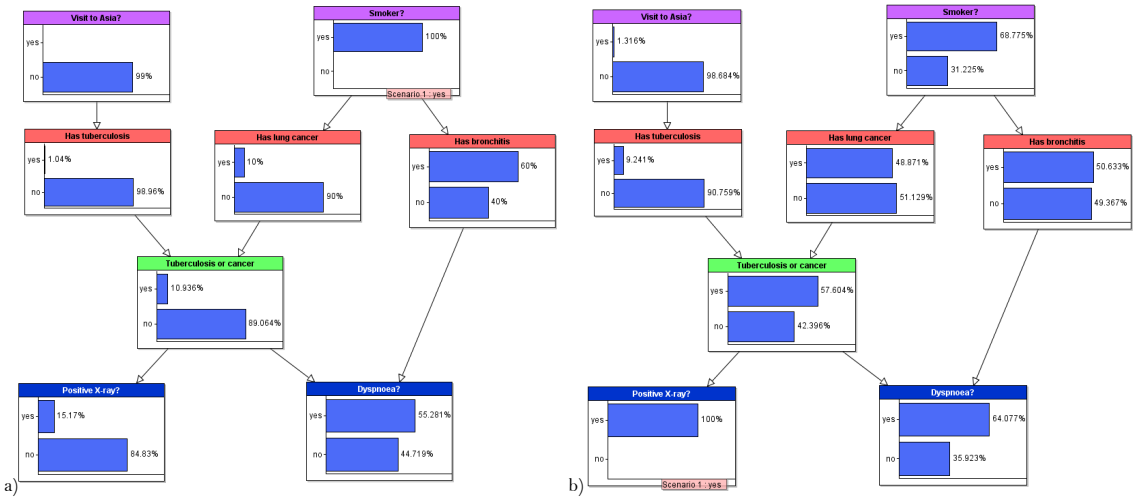

Figure 2.3: Asia BN inference after observing (a) that the patient is a smoker (b) that the patient's X-ray is positive

In case the relationships among the variables are causal, which is not necessary when we reason from observations, scenario (1) is known as causal reasoning, while scenario (2) is known as diagnostic reasoning. A particular case of diagnostic reasoning is a phenomenon called 'explaining away' [206], also known as 'discounting' [118], [178]. Explaining away can occur when a child node has more than one independent parent nodes. If the child node occurs, the probability of each of the parent nodes increases (diagnostic reasoning). But if

one of the parents is known to have occurred as well, then the probabilities of the others go down. This is because one explanation for the child is sufficient. Using the Asia BN, observing a positive X-ray increases the likelihood of lung cancer but also the likelihood of tuberculosis, as this can be also the cause of a positive X-ray. If we know now that the patient had tuberculosis, then the likelihood of cancer will decrease, as tuberculosis alone is sufficient for explaining a positive X-ray.

2.5.2 Interventional Reasoning

Reasoning from observations describes a joint distribution over possible observed events but says nothing about what will happen if an intervention occurs [274]. Reasoning through interventions can also be done in BNs, but only when the relationships among the variables are causal/ influential. The presence of cause-effect relationships is important, as in interventional reasoning we want to know the effect of an externally imposed intervention. An intervention is an exogenous action that fixes the state of the variable that we intervene upon and makes it independent of its causes [207], [250], [208]. Contrary to reasoning from observations, interventional reasoning does not allow diagnostic reasoning from the intervened variable [94]. For instance, when we observe a high body temperature on the thermometer, we can argue that we have a fever. On the other hand, if we arbitrary start rubbing the thermometer to reach a specific temperature, then we can no longer argue that we have a fever. According to Pearl, an externally imposed intervention is presented using the 'do operator'. For instance, using the previous example, the probability of having fever given that we observe a high body temperature on the thermometer is presented as *P(Fever = Yes | Thermometer = High Body Temperature)*. On the other hand, when we intervene on the thermometer, then the likelihood of having a fever is presented as *P(Fever = Yes | do(Thermometer = High Body Temperature))*. The process of making the intervened variable independent of its causes by removing all the edges pointing towards that variable is characterised by Pearl as 'graph surgery'. The interventions described so far, which fix the variable that we intervene upon, are known as 'atomic', 'strong', 'hard', 'perfect', 'deterministic' or 'independent'.

However, it is not always possible to have a 'hard' intervention. For instance, in medicine we cannot directly intervene on a specific disease or symptom, but we can indirectly intervene through a treatment. However, externally imposed a treatment does not make the

disease independent of its other causes. Consider the example shown in Figure 2.4a. Imagine that we want to intervene on the heart disease. We cannot perform a 'hard' intervention and fix its value. However, we can intervene on it indirectly by taking the appropriate medication. Fixing the state of medication to "Yes" makes the treatment independent of its cause, but the distribution of heart disease remains dependent of its causes, such as diet and family history Figure 2.4b. Such interventions have been called 'weak', 'soft', 'parametric', 'imperfect', 'dependent' or 'stochastic' [274], [66], [129], [131], [169]. These 'soft' interventions can arise for various reasons. Sometimes, it is not possible to perform a 'hard' intervention. For instance, it is not possible to make a behavioural or mental state independent of its other causes [180]. Sometimes, an intervention may have the ability to influence the state of the intervened variable, but it fails (e.g a drug does not influence a patient's condition). These interventions are called unreliable [64], [65], [169]. Finally, a 'soft' intervention may arise when the cost of a 'hard' intervention is too high or it is unethical.

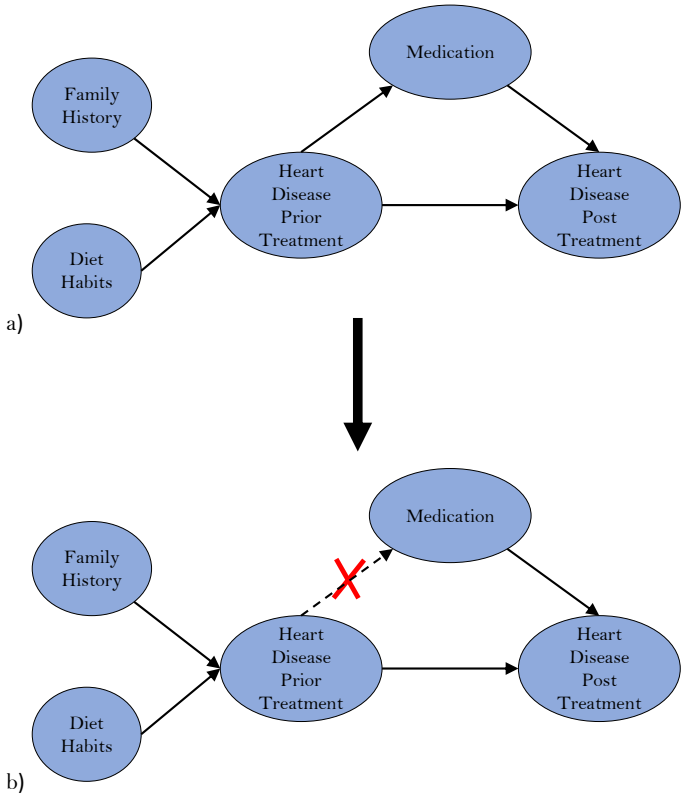

Figure 2.4: An example of a 'soft' intervention: a) a simple heart disease BN, b) intervening on the heart disease indirectly through the medication

Many researchers are sceptic about interventions. However, interventions can be traced

back to Fisher's analysis of experimental methods [78]. Statisticians have long relied on intervention to ground causal inference. In The Design of Experiments, Sir Ronald Fisher considers one treatment variable and one or more effect variables. This approach has since been extended to include multiple treatment and effect variables in experimental designs such as factor experiments. Randomly assigning participants (intervention) to experimental and control groups creates independence between the independent variable and possible confounds.

2.5.3 Counterfactual Reasoning

Counterfactual reasoning is about what would have happened if events other than the ones we are currently observing had happened. Considering 'contrary-to-facts' scenarios means imagining alternatives to reality. Although sometimes claimed otherwise [51], counterfactual reasoning is natural, and it is what makes human mind special [244]. In BNs, counterfactual reasoning combines observations and interventions. The actual word is modelled using observations, while the imaginary counterfactual world is altered using interventions. The main difference between counterfactuals and interventions is that for the former we know the values that some or all the variables had in the actual world. In contrast, when we intervene in a system, we do not know the values of the downstream variables in the network yet. There are two main approaches for counterfactual reasoning with BNs; the pruning theory introduced by Pearl [208] and the minimal-network theory proposed by Hiddlestone [103]. There are other approaches for performing counterfactual reasoning with BNs [154], but those two are the most widely used and discussed in the literature.

In pruning theory, Pearl suggested three main steps: 1) first we set the values of the observed variables to their current state, 2) then we apply the 'do operator' to the variables in the if-part of the counterfactual and 3) we see the prediction of the then-part of the counterfactual. Consider the following scenario (Figure 2.5a from [208]); we have two riflemen R_1 and R_2 that based only on the signal of their captain C, they shoot the prisoner D. In the actual world, we observe that the prisoner is dead, which makes certain that the captain gave the order and that both riflemen shot (Figure 2.5b). In the counterfactual world we want to see whether the prisoner would have survived if the riflemen R_1 had not shot. In Figure 2.5c we intervene on the variable R_1 and we force the rifleman not to shoot. That makes R_1 independent of whether the captain C gave a signal or not. In the counterfactual

world, we do not allow backtracking reasoning from R_1, so C stays intact (captain gave the signal). As a result, the prisoner is dead in the counterfactual world as well, because rifleman R_2 shot (Figure 2.5d).

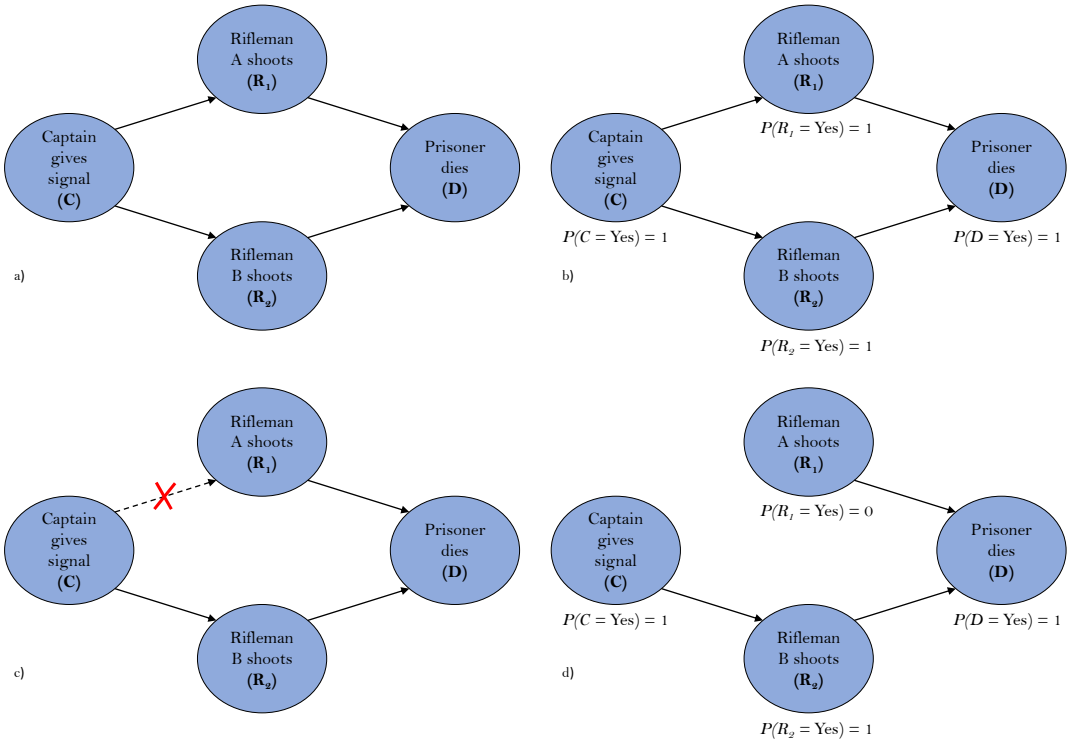

Figure 2.5: The process of counterfactual reasoning following pruning theory: (a) the BN without observations, (b) representation of the actual world, (c) intervening, (d) counterfactual world

Minimal-network theory, proposed by Hiddleston, is an alternative approach that assumes that the 'graph surgery' is not used. Again, the variables in the if-part of the counterfactual are updated. However, in contrast to the pruning theory, minimal-network theory assumes that causal principles are not disrupted. So, the counterfactual world is minimally different from the actual world. Hence, backtracking inference is permitted. Using the above example, forcing rifleman R_1 not to shoot implies that the captain did not give the order and as a result rifleman R_2 did not shoot either. Consequently, in contrast to pruning theory, the prisoner survives in the counterfactual world (Figure 2.6).

Many studies of behaviour have investigated how people perform counterfactual reasoning and tried to compare the two approaches, without however having a consistent conclusion [245]. Those studies investigated only humans' counterfactual thinking and they were not

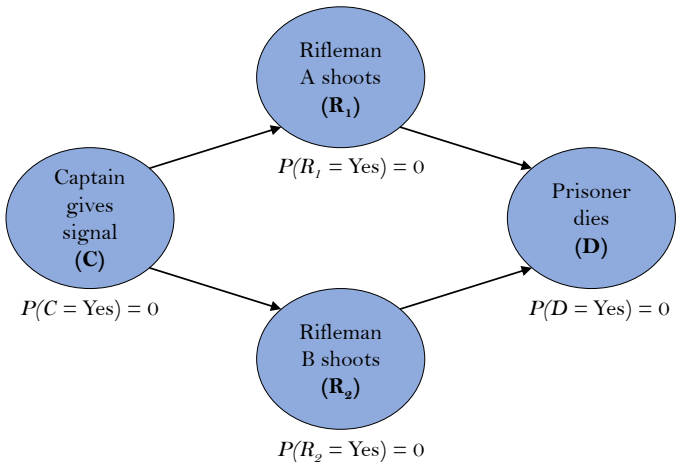

Figure 2.6: Counterfactual world created by minimal-network theory

concerned about probability theory. Sloman and Lagnado found that people's counterfactual judgement is closer to the pruning theory [243]. However, small changes on the questions led to different results. Thus, their results were difficult to be generalised. In contrast, Rips found that people perform backtracking inference when they reason about counterfactuals [221], [67]. However, the support on the minimal-network theory was not very strong. Similar results were found also in [55]. Finally, Gerstenberg et al. believe that people sometimes reason about counterfactuals using the pruning theory and sometimes using the minimal-network theory [85], [86]. Their experiments revealed that backtracking inference is highly related to the order the counterfactual questions were asked. Their conclusion was that people's counterfactual reasoning is closer to minimal-network theory when they were asked to consider a possible cause of the counterfactual state first. In contrast, when they were asked to consider the effect of a counterfactual state first, their reasoning followed the pruning theory.

2.6 Development of Time-Based BNs

The above types of reasoning can assist different aspects of decision making. However, decision making is not a one-time activity, but an evolving process. This section reviews some of the most important time-based BN methods that have been proposed over the years to capture the dynamic process of decision making.

2.6.1 Dynamic BN

A widely known approach to temporal reasoning with BNs is the Dynamic BN (DBN). DBNs extend BNs to model environments that change over time [187]. The idea of DBNs, referred to as temporal probabilistic networks, was first introduced by Dean and Kanazawa in 1989 [53]. Since then, many scientists have studied DBNs [49], [121], [187], [188], which exist in many variants. We start by describing the DBN as described in Murphy's thesis [181], published in 2002, since this is widely known. In the following sections, we go on to describe extensions to DBN (mostly known by other names) and also mention some of the earlier variants, where relevant.

The term 'Dynamic' denotes that the values of the variables change over time, and not that the model's structure itself changes over time. According to Murphy, the first assumption of DBNs is the discretisation of time into a set of fixed time slices. Time slices are discrete intervals that are spaced with a predetermined time granularity Δ [127]. For instance, if we are interested in monitoring the patient's condition every day, then $\Delta = 24h$. In a 2-time slice DBN some of the edges are inter-time-slice edges going between time slices, whereas others are intra-time-slice edges, connecting variables in the same time slice [127]. As a result, we distinguish between two types of relationship in a DBN: transitional relations that capture dependence among variables between different time slices, and local relations that capture dependence between variables within the same time slice (Figure 2.7).

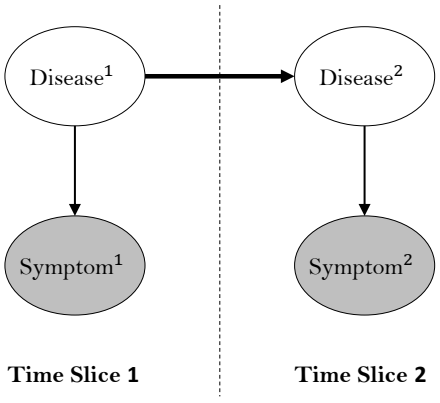

Figure 2.7: A 2-time slice DBN: grey nodes are observed, thin edges are intra-time-slice edges that capture local relations and the bold edge is an inter-time-slice edge that captures transitional relations

Imagine that we discretise time into $t = 0, \ldots T$. The distribution of the variable X can be

parameterised in a direction consistent with time such as:

$$P(X^{(0:T)}) = \prod_{t=0}^{T-1} P(X^{t+1}|X^{(0:t)}) \tag{2.5}$$

From the equation 2.5, we can conclude that the distribution over time is the product of conditional distributions for the variables in each time slice given the previous ones. Thus, the future is conditionally independent of the past when the present is known. This is known as the Markov process which indicates that for all $t > 0, (X^{t+1} \perp X^{0:(t-1)} \mid X^t)$. It may be noted that this property is like d-separation in case of a serial connection (see Section 2.4). DBNs use the Markov assumption to simplify equation 2.5, such as:

$$P(X) = \prod_{t=0}^{T-1} P(X^{t+1}|X^t) \tag{2.6}$$

However, this assumption can be relaxed, and semi-Markov models can also be considered. Although, we simplified equation 2.5, we still have many conditional probabilities to learn when many time slices are used. For that reason, another assumption made is the assumption of stationary transitions, also known as homogeneous or time invariant. In other words, the structure and parameters of a DBN are fixed throughout the time such as $P(X^{t+1}|X^t)$ is the same for all t. Thus, we can say that DBN is a compact representation from which we can generate an infinite set of BNs, one for each time slice.

The discretisation of time, the Markovian assumption and the stationarity make the use of DBNs easier, as they allow us to represent the probability distribution over infinite time slices very compactly. We only need an initial distribution and a transition model that represents the conditional probability distribution. However, those assumption might not be always true. For example, data cannot be always discretised, or the structure of a BN and its parameters may change over time. The following sections explain how those assumptions have been tackled over the years.

2.6.2 Time-Based BN with no Fixed Time Discretisation

DBNs are a good choice for domains where data is naturally time-sliced and where questions about events occurring between time points are not relevant. While discretisation is often indeed reasonable, there are situations in which a discretisation of a fixed granularity or even a natural discretisation is not available. For instance, if a system is composed of processes that evolve at different time granularities and we discretise time at the finest

possible granularity, then data on some time slices might be missing and conditional probabilities will be hard to estimate. As a result, the learning problem can quickly become intractable. On the other hand, if we discretise time too coarsely, we lose information.

Different variants of DBNs exist that relax the assumption of fixed time discretisation. For instance, Dean and Kanazawa proposed a node delta-t for each time slice to avoid same time step [53]. In the context of robot monitoring, Nicholson proposed a new DBN slice to be added when a sensor observation indicated an event may have occurred [188]. A new type of time-based model, called continuous time BN (CTBN), was also developed to avoid time discretisation [193], [190]. CTBNs describe a continuous time stationary Markov process with finitely many states. A CTBN consists of two main components: (1) an initial probability distribution, specified as a BN and (2) a continuous transitional model that specifies the behaviour of each variable as a function of its parents. A continuous transitional model is a directed, possible cyclic graph, with a conditional intensity matrix where the (i, j) entry gives the intensity of transitioning from state i to state j. The CTBN specifies, at any given point in time, the distribution over two aspects: when a variable change its value and the next value it takes. A lot of research has been done to explain the learning [194], inference process [192], [71] and the distributions that can be used in CTBNs [191]. Finally, few more extensions and applications of CTBNs have been also proposed [89], [70], [238], [84], [278].

Apart from CTBNs, other approaches were developed to handle time discretisation. Arroyo proposed Temporal Nodes BNs (TNBNs) [9]. In a TNBN, each node represents an event or a state change of a variable that can happen only once and an arc corresponds to a causal-temporal relation. In a TNBN there are two types of nodes: (1) instantaneous events that have no temporal intervals, and (2) temporal nodes that indicate both the state and the time when the event happened. Figure 2.8 shows a simple TNBN. In this example, head injury is an instantaneous event and unconscious is a temporal node with states 'Yes' and 'No' and with time intervals [0-15] and [15-30]. The temporal intervals can differ in number and size for each temporal node, allowing multiple granularities. This approach works for discrete data and each variable represents events that can happen only once. However, this is not always true. For example, an injured patient can be given blood products many times during his hospitalisation. Ramati Shahar proposed Irregular-Time BNs (ITBNs) that

generalise DBNs such that the granularity between each time slice can be irregular [215]. The time difference between consecutive slices may vary according to the available data and inference needs. Finally, Liu et al. proposed hybrid time BNs (HTBNs) [150], [151]. HTBNs are inspired by both discrete-time and continuous-time BNs and they facilitate modelling the dynamics of both irregularly-timed random variables and random variables whose evolution is naturally described by discrete time.

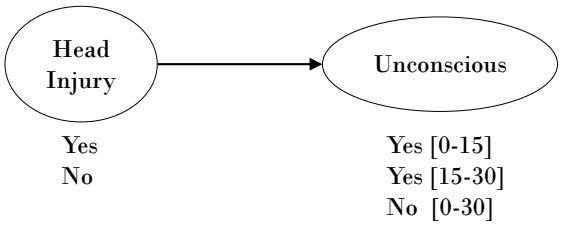

Figure 2.8: A TNBN example

2.6.3 Non-Stationary Time-Based BN

Except for time discretisation, another matter that drew researchers' attention was the assumption of stationarity. Under the assumption of stationary transitions, a DBN is effectively constructed by unrolling a BN in time, and the model learning procedure is greatly simplified. However, this assumption limits the power of DBN in modelling many non-stationary sequences, where the relationships among variables change from time to time. Such non-stationary sequences may arise in all aspects of our life such as: the gene interactions in different stages of a life circle, the stock prices in different economic periods, the treatment of an acute medical condition in different medical facilities, the monitoring of chronic conditions in different age periods. The assumption of stationarity is therefore too restrictive in many circumstances and had led to the development of a new type of time-based BN called non-stationary DBN (nsDBN). nsDBNs assume that the underlying data generation process may change over time, so the structure and/or parameters of the model evolve over time as well (Figure 2.9).

Many different approaches of nsDBNs have been developed over the years. Talih and Hengartner proposed a nsDBN where the number of the time slices is known apriori and the network structure between different time slices is restricted to changing at most a single

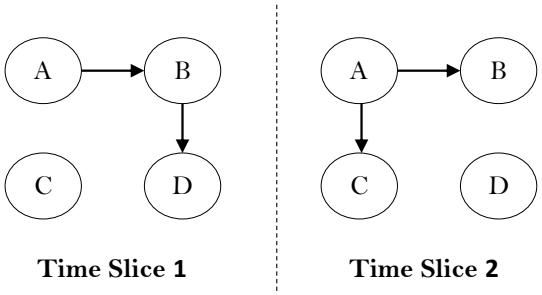

Figure 2.9: nsDBN example (based on Robinson and Hartemink [222])

edge [257]. Xuan and Murphy proposed a nsDBN where a separate structure is created for each time slice. The structure and number of time slices are learned from data [277]. The nsDBNs proposed in [257], [277] are based in correlations among their set of fixed variables and not conditional dependencies as only undirected edges are permitted. In addition, they both assume that the networks in each time slice are independent, preventing data and parameters from being shared between time slices. Lebre proposed an alternative continuous nsDBN, which is more flexible and allows the network structure to vary among the time slices [143]. However, no information sharing is allowed across time. The number of time slices and the time change points are inferred from data. Robinson and Hartemink proposed a discrete nsDBN (Figure 2.9), which allows for different structures in different time slices [223], [222]. This approach allows the conditional dependence structure to change over time. Again, the number of time slices and the time change points are inferred from data. Grzegorczyk and Husmeier proposed a continuous nsDBN, in which only the parameters can vary, with a common network structure providing information sharing among time slices [92]. Dondelinger et al. proposed a method that tries to overcome some of the shortcomings of the existing methods [60]: (1) avoid the information loss inherent in a discretisation of the data (as opposed to [223]), (2) allow the network structure to change among time slices, leading to greater model flexibility (as opposed to [92]), and (3) introduce information sharing among time slice (as opposed to [143]). Jia Huan proposed a new nsDBN method that decomposes the whole time span into several time slices and then reconstructs a DBN within each time slice, assuming that the network structure for the time points within the time slice is the same [112]. Finally, nsDBNs are also known as time varying DBNs (TV-DBNs). This terminology was introduced by Song et al. for modelling the varying network structure of gene expressions [248]. Wang et al. proposed also a TV-DBN for online inference of the underlying distribution of non-stationary sequences [272].

2.6.4 Knowledge Gap

To sum up, different time-based BNs have been proposed over the years. DBNs are the most applied as they are easy to build, train and use. However, they are based on two strong assumptions; time discretisation and stationary transitions. These assumptions are not true in many applications. Several approaches have been proposed to overcome these assumptions. However, most of the described methods, use data to estimate either fixed or flexible granularities. This can be useful when we have rich and high-quality data, with a clear passing of time, which is not always the case. Thus, using data to estimate the granularity may lead to unnecessary time slices that are not relevant with how the model is intended to be used. CTBNs can be adjusted to the decision making timeline but learning and interpreting them, especially the intensity matrices, is a difficult task. Many methods try to overcome the assumption of stationarity by allowing the structure and/or the parameters of the model to change over time. Most of these methods allow one or more edges to change among a predefined set of variables. The fixed set of variables represents the available data. However, in many problems, especially in medicine, information that should be included in the model may not be captured. In the following chapter, we review the application of the above techniques in medical problems and we investigate the barriers that they may face in assisting clinical decision making.

Chapter 3

Useful Clinical Decision Support Models

This chapter focuses on how CDS models can assist clinical decision making. First, we present some medical BN applications, as well as their limitations, and then we investigate why many of the developed models have not been used in clinical practice. The limitations described in this chapter lead to the contributory Chapters 5 and 7.

3.1 Introduction

Clinical decisions can be grouped into three main categories: (1) diagnosis, (2) prognosis and (3) treatment. During diagnosis, clinicians evaluate the patient's symptoms and signs and decide which disease explains them better. In prognosis, clinicians use their knowledge, experience and patient's characteristics to predict the outcome of the disease and the frequency with which it is expected to occur. Finally, clinicians evaluate patient's characteristics and history to decide the appropriate treatment. Clinicians take thousands of decisions of all types during their career.

In recent years, advances in diagnostic tests and in understanding both the causes of diseases and the benefits of different treatment options have generated more and more evidence that needs to be considered in clinical decisions. However, clinicians may have difficulties combining all the available evidence to make an appropriate decision [27]. In some types of care, clinicians need to take a decision very quickly [79]. For instance, a surgeon in the ED takes several decisions under time pressure, such as whether to wait for the computed tomography scan results or to go straight to theatre as the patient's condition is critical. When time is pressuring, clinicians rely mainly on a hunch and on a limited amount of

evidence. In both cases, clinicians reason under uncertainty by combining appropriately all the available information.

Many ways to assist clinical decision making have been suggested [251]. One way to assist clinical decision making is to use CDS models [1], [239], [61], [18], [205], [2], [45], [147]. A CDS model can be a scoring system, a rule-based system, a regression model, a neural network or a decision tree [2]. Although each type offers advantages (e.g. simplicity or ease of inference), not all are able to capture the uncertain nature of medicine in contrast to BNs, which as explained in Chapter 2, offer a natural way to represent the uncertainties involved in medicine when dealing with diagnosis, prognosis and treatment. In addition, one of the main advantages of BNs is that they can represent both the data and clinician's knowledge and reasoning. Most of the other specified CDS models are largely data-driven, a fact that can be problematic when developing medical models. Another recently proposed graphical CDS model is the chain event graph, which is a compact form of event tree model [247], [15] that has also a dynamic counterpart [16]. Despite its potential advantages in many staged-care medical problems, a drawback is that a chain event graph becomes hard to understand in large problems with more than 20 states, this may explain why chain event graphs have not yet become as widely known or supported as BNs. For all the described reasons, we will focus from now on only on CDS BN models.

In this chapter, we review different types of BNs that have been developed in medicine. We investigate their benefits, but also their limitations in practice for improving decision making. The remainder of this chapter is organised as follows: in Section 3.2, we present various medical BN applications, as well as their limitations. In Section 3.3, we give reasons why some models are not as useful for practical decision support as might be hoped.

3.2 Bayesian Networks in Medicine

Medicine has been one of the most popular application areas for BNs. Their popularity in medicine lies in their ability to model complex problems, where a significant degree of uncertainty is involved, to combine different sources of information such as data and experts' judgement, to have a graphical structure that facilitates their explanation and interpretability, to model causal interventions and to reason both diagnostically and prognostically. Given all these benefits, many BNs have been develop over the last 20 years to assist

clinicians [157], [199]. A representative, but not exhaustive, sample is presented in Table 3.1. Regardless the medical problem, the main clinical decisions that these applications intend to assist are: (1) diagnosis, (2) prognosis, and (3) treatment. The described BNs are built using knowledge engineering methods, data, or a combination of both. For BN built from knowledge, a further develop is to use a template approach or to distinguish between different kinds of variables; some examples of these techniques have been given in Section 2.3.

As it is shown in Table 3.1, most of the BNs are static models, either with no or an implicit time element introduced in the model's variables. In static BNs, clinical decisions are considered as a one-time activity. However, this might be too restricted. Many times, clinicians take several critical decisions in different stages of the patient's care. Suppose for instance that a young female with acute abdominal pain arrives in the ED. After the initial examination, the clinician finds out that the patient has a right lower quadrant pain. The clinician suspects either appendicitis or an ovarian pathology, so he decides to send the patient for an ultra sound scan test. The results show the presence of an inflamed appendix. Now based on the new information, the clinician decides to send the patient to theatre for an appendicectomy. This scenario illustrates the evolving process of gathering clinical information, and the dynamic nature of clinical decision making. In these cases, static BNs are not always appropriate.

There are several approaches to modelling the dynamic process of decision making and reasoning in medicine [10], [3], [202]. While BNs have been used as CDS models for over two decades, their temporal extension found its way into medicine more recently. In section 2.6 we presented the most important time-based BNs. The most well-known and used time-based BNs in medicine is the DBNs, as they are easy to build, train and use [182]. However, in many medical problems data are not always naturally time-sliced or decisions are not taken at fixed regular time points. In addition, having a fixed structure and parameters is too restricted in medical applications, where the symptoms, diagnostic tests and treatment capabilities might vary a lot at each time point. As explained in Section 2.6, many methods try to relax the assumptions of time discretisation and stationarity. However, most of the methods identify the time points and the structure and parameters of the model from data. This can be possible when we have rich and high-quality data, which is rarely true

in medicine. All these factors justify why the described methods are not always applicable in many medical problems. Some medical applications of the time-based BNs described in section 2.6 can be found in Table 3.1.

Table 3.1: BN applications in medicine

Publication	**Medical Condition**	**Task**	**Type**	**Data**	**Knowledge Engineering**
Magrini et al. [161]	Acute cardiopulmonary diseases	Diagnosis	Static	P	V,A,P
Yet et al. [281]	Anticoagulant treatment	Treatment	Dynamic	P	V,A,P
McGeachie et al. [168]	Arteriosclerosis	Diagnosis	Static	V,A,P	-
Burnside et al. [33]	Breast cancer	Diagnosis	Static	-	V,A,P
Wang et al. [271], Cruz-Ramirez et al. [46]	Breast cancer	Diagnosis	Static	V,A,P	-
Van Gerven et al. [265]	Carcinoid tumour	Prognosis	DBN	P	V,A
Verduijn et al. [267]	Cardiac surgery	Prognosis	Static (IT)	V,A,P	-
Gatti et al. [84]	Cardiogenic heart failure	Diagnosis	CTBN	-	V,A,P
Onisko et al. [201]	Cervical cancer	Diagnosis, Prognosis	DBN	V,A,P	V,A
Yet et al. [282]	Coagulopathy	Prognosis	Static	P	V,A
Nissan et al. [189]	Colorectal cancer	Prognosis	Static	V,A,P	-
Seixas et al. [234]	Dementia, Alzheimer's disease, mild cognitive impairment	Diagnosis	Static	V,P	A

Note: A = arc, V = variable, P = parameter, IT: implicit time introduced in the model's variables

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Table 3.1: BN applications in medicine

Publication	**Medical Condition**	**Task**	**Type**	**Data**	**Knowledge Engineering**
Celi et al. [38]	Fluid requirements	Treatment	Static (IT)	V,A,P	-
Zou et al. [284]	Gene regulatory	Prognosis	DBN	V,A,P	-
Ramati et al. [215]	Glucose level	Monitoring	ITBN	V,A,P	-
Diez et al. [57]	Heart diseases	Diagnosis	Static	-	V,A,P
Cai et al. [37]	Hepatocellular carcinoma	Prognosis	Static (IT)	V,A,P	-
Onisko et al. [200], Wasyluk et al. [273]	Liver disorders	Diagnosis	Static	P	V,A
Sesen et al. [236], [235], [237]	Lung cancer care	Prognosis, Treatment	Static (IT)	V,A,P	A
Sierra et al. [241]	Malignant skill melanoma	Prognosis	TNBN	V,A,P	-
Rose et al. [225]	Monitoring patients treated by haemodialysis	Diagnosis/ Monitoring	DBN	-	V,A,P
Nordmann et al. [195]	Night-time intraocular pressure	Prognosis	Static (IT)	V,A,P	-
Luo et al. [159]	Non-small-cell lung cance	Prognosis	Static (IT)	V,A,P	-
Ltifi et al. [153]	Nosocomial infections	Prognosis	DBN	V,A,P	-
Himes et al. [105]	Obstructive pulmonary disease	Prognosis	Static	V,A,P	-

Note: A = arc, V = variable, P = parameter, IT: implicit time introduced in the model's variables

Continued on Next Page...

Table 3.1: BN applications in medicine

Publication	**Medical Condition**	**Task**	**Type**	**Data**	**Knowledge Engineering**
Peelen et al. [209]	Organ failure	Prognosis	DBN	P	V,A
Sandri et al. [231]	Organ failure	Prognosis	DBN	P	V,A
Heckerman et al. [100], [99], [98]	Pathologic disorders	Diagnosis	Static	-	V,A,P
Beinlich et al. [19]	Patient disorders in intensive care	Diagnosis	Static	P	V,A,P
Klammer et al. [122]	Peptide fragmentation	Modeling	DBN	V,A,P	-
Moreira et al. [177]	Preeclampsia	Diagnosis	Static	P	V,A,P
Lacave et al. [139]	Prostate cancer	Diagnosis	Static	P	V,A,P
Curiac et al. [47]	Psychiatric diseases	Diagnosis	Static	V,A,P	-
Hulst et al. [110]	Psychology	Modeling	DBN	V,A,P	-
Dagum et al. [48]	Sleep apnoea	Prognosis	DBN	V,A,P	-
Kline et al. [125]	Venous thromboembolism	Prognosis	Static (IT)	V,A,P	-
Lucas et al. [158], Schurink et al. [233], Visscher et al. [268], Charitos et al. [44]	Ventilator-associated pneumonia	Diagnosis	DBN	P	V,A

3.2.1 Challenges to Overcome

The use of BNs has been extended to address medical problems in which temporal reasoning is modelled. Many time-based BNs have been proposed to assist the dynamic process of clinical decision making, with DBNs being the most widely used. However, there are some challenging tasks that remain, such as modelling an evolving condition when the available data are limited, capturing and assisting clinical decision making in irregular time points following clinician's decision process and not data availability. In Chapter 5, we propose a method to model an acute medical condition, described in Chapter 4, that evolves rapidly over a short timescale. The proposed method considers the progressive way clinicians gather information and take decisions.

Even if a method is applicable, and a model is developed, this does not automatically indicate that is going to be used in clinical practice. The next section explains the reasons why a developed model might not be used in practice to support clinical decision making.

3.3 Clinical Decision Support

As presented above, many BNs have been developed in medicine [156]. However, very few of them have been actually used in practice to support decision making. Having an accurate BN that models the medical problem is important, but it is not enough to make it useful. It seems that there is a gap between developing an accurate model and having a useful model that can have an actual impact on the clinical decision making process. Acknowledging that problem, many researchers have investigated the potential reasons [276], [172], [24], [216], [261], [176], [174]. According to the existing literature, the main characteristics of a useful model are: (1) Clinical Benefit, (2) Accuracy, (3) Clinical Credibility, (4) Generalisability, and (5) Impact.

The first factor is the clinical benefit. A clinical benefit can be a faster prognosis, better treatment strategies, an improved patient's outcome, a better and faster recovery or even a lower cost. It is important to know the existing situation and if there is any margin of improvement. If there is no potential of a clinical benefit, then a BN is never going to be useful. The second factor is the statistical accuracy of the model [28], [266], [6], [253]. The accuracy reveals the predictive quality of the model. However, an accurate prediction

should not be confused with a decision. An accurate model that it is not clinically credible is not going to be used to assist decision making. A developed and validated model is clinically credible when its logic is clear, and the model appears to describe what it intends to describe. In addition, a BN cannot be accepted if it has not been proved to work on other populations. Thus, the generalisability of the model is about testing its accuracy using datasets other than the original training dataset (domain, external, temporal validation) [24], [6], [174]. The final characteristic of a useful model is its impact. The impact of the model represents its clinical effectiveness [217], [216], [114], [115]). An impact analysis is a trial that can show whether the tool can have a long-term implementation to assist decision making or there are some barriers that we need to resolve first.

One of the components of the clinical credibility of the model, which is very often neglected, is its trustworthiness. Clinicians are less likely to use a model if they do not trust it. The predictive accuracy and generalisability are important, but they are not the only type of trust. A clinician is less likely to trust a model that he does not understand. In this section, we describe the existing approaches for making a BN more trustworthy.

3.3.1 What Needs to be Explained?

We cannot trust a model if we cannot understand it. Generally, we understand something that it is explained to us using simple and familiar terms. An explanation is a process of understanding a statement by providing causal connections to known facts [166]. However, different statements require different explanations. Lacave reviewed the explanation methods in BNs [138], distinguishing the following different focuses of an explanation:

1. Explanation of the model: we want to explain how the structure and parameters of the model relate to the domain knowledge.

2. Explanation of the evidence: we want to explain the evidence variables by determining the most likely values of the unobserved variables (e.g. the disease that best explains the symptoms).

3. Explanation of reasoning: we want to explain how the evidence leads to a prediction for one or more unobserved variables.

All the three types of explanation can be useful to a clinician. However, here we want to increase the clinical credibility of the model, by making its prediction more trustworthy. The

prediction of a BN is presented as a probability, with no indication of the reasoning behind the predictive. The model only shows that, based on the patient's information entered by the clinician, the outcome will occur with a given probability. As a result, an explanation of the model's reasoning that provides a justification of the results can be beneficial. The form of such an explanation can be illustrated by the following scenario:

> *A doctor uses a BN that predicts the likelihood of coagulopathy*[1] *in traumatically injured patients. He enters the evidence and the model predicts that the patient is 8.7 times more likely to become coagulopathic than an average trauma patient. When asked to explain, the system informs him that despite the positive effects of the absence of a long bone and pelvic fracture and a negative FAST scan*[2]*, the likelihood of coagulopathy increased because of the thoracic fracture, the high energy of the injury, a base excess*[3] *of -14, a Glasgow Coma Scale*[4] *(GCS) of 4 and the administration of more than 500ml of fluids. In complicated cases, just explaining the significant positive and negative causes may not be sufficient. The system can further explain that the evidence affected the prediction of coagulopathy through the unobserved variables tissue injury and tissue perfusion.*

This example shows the basic components of an explanation. First, the explanation has a target, here 'coagulopathy'. Then the most significant evidence variables that support or contradict the prediction are presented. For more details, the explanation introduces some unobserved intermediate variables through which the information flows and describes how they are affected by the evidence.

3.3.2 Methods for Explaining Reasoning in Bayesian Networks

Several methods of explaining the reasoning in a BN have been proposed. Common elements are i) how to measure the impact of the evidence variables on the target and ii) determine which variables need to be included in the explanation, iii) how to distinguish between supporting and conflicting evidence and finally iv) how to explain the flow of information from evidence variables to the target, described as 'chains of reasoning'. Our review

[1] Coagulopathy is a bleeding disorder.

[2] FAST scan uses ultrasound to check for internal bleeding.

[3] Using base excess we check for respiratory problems.

[4] GCS assesses the consciousness.

is focused on papers that cover the parts (i) - (iv) described before and are widely discussed in the literature. Other methods, such as [279], [260], [269], which lack the described parts are not reviewed here. A more in depth literature review can be found in [138].

The Impact of Evidence

Not all the evidence has equal impact on the target variable. Measuring the impact involves assessing the change in the probability distribution of the target produced by the evidence. There are different distributions that can be compared and different measures to do that. The explanation system INSITE, developed by Suermondt, uses the Kullback Leibler (KL) divergence between the posterior of the target with all the evidence and the posterior of the target when each evidence (one-way analysis) or a subset of evidence (multi-way analysis) has been temporarily removed [254]. Exact multiway analysis for the best subset of evidence is time consuming as it is exponential to the number of evidence variables. In addition, the KL divergence is not well defined when the denominator is 0. Chajewska and Draper address the computational complexity with more flexible requirements for the size of the explanation set and the significance of the impact that each evidence variable has on the target [39]. They also point out that the prior probability of the target needs to be considered. The explanation system BANTER measures the difference between the prior and the posterior of the target for each evidence variable on its own [93]. However, this simplification can be misleading sometimes as it neglects the rest of the available evidence variables. Madigan et al. assess the impact using Good's weights of evidence [88], evaluated incrementally as the user instantiates each evidence variable; a binary target is assumed, and the calculated weights depend on the order the evidence is entered [160].

Setting a Threshold for Significant Evidence

The explanation should only include the evidence variable with the greatest impact. Many ways have been proposed to find an appropriate impact threshold. A simple approach is for the end user to choose a threshold [39]. However, even if the end-user has the domain knowledge needed, it is hard for him to express this in terms of the range of the distance measurement. Alternatively, a fixed threshold is chosen by the model builder [93] or the impact of all the evidence variables is presented, from the largest to the smallest, without a threshold [256]. This can make the explanation very complex when there are many evidence variables. INSITE proposes an indirect way for the user to choose a threshold.

Instead of choosing an appropriate threshold for the distance measurement, the user specifies an 'indifference' range for the posterior of the target; changes outside this range are significant and the corresponding threshold can be calculated. This approach combines the users' domain knowledge, given as the range of indifference on the probability, and the characteristics of the distance measure. However, this range may need to be changed for each query and it is still not easy for the end user to do this, especially when the target variable is continuous, or the decision tool is being used under time pressure.

Supporting and Conflicting Evidence

We also want to know whether each evidence variable supports or conflicts with the overall change predicted by the model. INSITE introduced the idea of conflict analysis in an explanation, looking at whether removing an evidence variable shifts the posterior of the target in the same direction as the change from the posterior with all the evidence to the prior when all the evidence is removed. However, this analysis is limited to binary variables. For non-binary variables mixed effects can occur, where the change for some states supports and for other states conflicts with the overall change. Madigan's use of the weight of evidence distinguishes between positive and negative effects, but it may depend on the order evidence is entered.

Chains of Reasoning

Evidence variables may be connected to the target by other variables in a 'chain of reasoning'. Choosing which of these variables to include in the explanation is difficult as there can be many such chains. INSITE generates a set of directed chains from each significant evidence variable to the target, and, by screening the effect the evidence has on each variable in each chain, it eliminates those chains that block the transmission of evidence. Additional screening is performed by removing arcs that link chains. BANTER selects the chains with the highest strengths and the minimum length (among chains with the same strength) by measuring the impact of every variable in the chain. The strength of the chains is given by the minimum impact of any of the variables in the chain. Madigan et al. screen the evidence chains by looking at the weight of evidence of every variable in a chain of reasoning. The weight of evidence for each variable relates to the ratio between the weights of the incoming and outgoing evidence. However, they only consider networks with a tree form, which have only a single path from an evidence variable to the target. Leersum tries to find a non-empty

set of intermediate variables that summarizes all the information between the evidence and the target. He looks at the weight of the edges using a Maximum-flow-minimum-cut theorem and then considers only the variables that are connected with the edges of the minimum cut, which is the minimum set of edges that makes the graph disconnected [145].

3.3.3 Challenges to Overcome

Explaining the reasoning of a CDS model, which as we argue is an important element of trust and clinical credibility, should be easier for BNs, since they are not black box models. Several approaches have been proposed to explain the reasoning of a BN. However, there are many situations where these methods cannot be applied. First, most of the described methods can be applied to BNs that include only discrete variables. Some of them are even restricted to binary variables only. However, most of the medical BNs include continuous nodes as well. In addition, most of the methods try to find the best explanation that can be time-consuming, especially for large BNs, which are common in medical applications. Finally, in some methods, the user input is required in different stages of the explanation. This can be problematic, especially in situations where there is a time pressure. In Chapter 7, we propose a method for developing an explanation of reasoning for CDS BN models that overcomes the above limitations and give a good explanation, but not necessarily the most complete one. A real clinical case study is used to illustrate the explanation. A small evaluation study is also conducted.

Chapter 4

Case Study: Modern Combat Trauma Care

This chapter introduces the necessary background knowledge related to the case study used in Chapters 5 and 6. The case study is about combat trauma care for traumatically injured soldiers.

4.1 Overview of the Case Study

This section gives a brief description of the modern combat trauma care and the clinical decision making process.

4.1.1 Combat Trauma Care

Military medicine worldwide shares a universal objective; to advance combat casualty care across all stages of the clinical care and save lives [36], [87]. A casualty encompasses those both killed and injured. Combat trauma casualties present a unique challenge and their emergent care and management require experience and expertise [20], [29], [87]. The overall objective of combat trauma care is to stabilise, evacuate, and return the soldier to duty as efficiently as possible. Most deployed military trauma systems of care are composed of levels of care that begin at point of wounding and continue through escalating roles of care with increasing capabilities. The capability of a medical facility describes the medical effect it can have, and it is described in terms of its size; both staffing a casualty capacity and the medical treatments it can provide. The deployed combat trauma system starts from self and buddy aid at the point of wounding at one end and at the other end includes home

nation reconstruction and rehabilitation services [34], [7]. A staged approach to combat trauma care includes five main roles of care (Figure 4.1). In order to simplify the use of this concept, they are referred to as Role 0-4. Each Role can be described as:

- *Role 0 - Basic and enhanced first aid*: Enhanced first aid plays a crucial role in soldier's survival. Bleeding, airway control and administering personal medical countermeasures for the most severely injured patients is doctrinally recommended to happen within ten minutes of wounding (the so-called platinum ten minutes). Initially, the first aid is self aid and/or buddy-buddy aid as show in in Figure 4.2.

- *Role 1 - Enhanced field care*: Within 1 hour of wounding, patients should receive enhanced field care (pre-hospital emergency care) in an appropriate clinical working environment. Role 1 can be a tent near the battlefield (Figure 4.3).

- *Role 2 - Damage control surgery*: Patients needing surgery should receive treatment in a facility manned and equipped for damage control surgery (DCS). DCS is a technique of surgery utilised to care for critically ill patients [226]. Depending on the specific operational circumstances, the aim should be to provide DCS within one hour, but no later than two hours of wounding. Acute medicine is the equivalent clinical capability for non-surgical emergencies. Both DCS and acute medicine should always be supported by a critical care unit Figure 4.4. These interventions are designed to stabilise the patient pending further medical evacuation.

- *Role 3 - In theatre surgery*: Further in-theatre surgery and enhanced diagnostics should be available within two hours of tactical evacuation from DCS/acute medicine for the severely injured. This role takes place in a fixed hospital where there is greater clinical capability and capacity (Figure 4.5).

- *Role 4 - Definitive hospital care*: Repatriation back to the UK at Queen Elizabeth Hospital in Birmingham.

For critically injured combat casualties, survival from trauma is associated with the time that has elapsed between injury and receiving a required intervention. Although rapid prehospital transport to a higher level of medical care is important, it is rather the timely administration of a needed intervention that is ultimately paramount [179]. The speed and quality of medical care can reduce the mortality and morbidity of casualties. The ideal is always to deliver expert care as soon as possible after wounding. In an effort to decrease

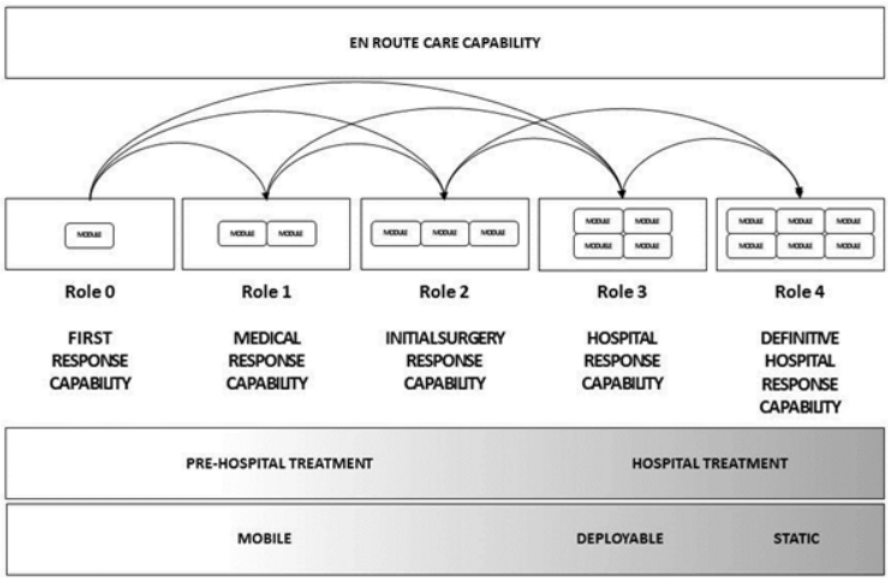

Figure 4.1: UK medical capabilities in the continuum of care (figure taken from [54])

time to life saving interventions the British Defence Medical Services (DMS) decided to deliver expert medical care as close to the point of wounding as practically possible. This was achieved using the Medical Emergency Response Team (MERT).

Depending on soldier's condition, military tactical environment and geographic distance the characteristics of MERT may change. For instance, in Afghanistan British DMS used an enhanced MERT which was 'enhanced' by the consultant doctor and a CH47 helicopter (Chinook). Because of the relatively small area of operation, British did not have their own Role 2 facility. So, the enhanced MERT acted as a bridge to get the casualty back to Role 3 and perform often life-saving treatments whilst on flight. In the next conflict, MERT could refer to a light wheeled road ambulance, a boat platform or an adapted tank ambulance without doctors on board.

4.1.2 Clinical Decision Making in Combat Trauma Care

In the prehospital setting (Roles 0 and 1), the combination of reduced prehospital transport time and increased treatment capabilities are likely contributors of casualty survival despite the increased severity and complexity of wounds [165], [26], [249], [212], [132], [133]. Haemorrhage mitigation and airway management are the most important decisions/ actions at this stage [62],[107], [40]. Role 0 is an unsafe environment. The first military action is to transfer the casualty and those providing care to an area of lower threat and perform some life-saving interventions. In Role 1 the environment is safer, but the decisions are similar:

Figure 4.2: Role 0 environment

This image was downloaded from https://www.telegraph.co.uk/news/worldnews/asia/afghanistan/9165695/Afghanistan-moment-Private-Stephen-Bainbridge-stepped-on-an-IED.html

control bleeding, control airway and evacuate the casualty.

The enhanced MERT picks up the soldier from Role 0 or 1 and flies him to the deployed hospital in Role 3. Here the environment is safer, and some treatments can be performed but still the capability is limited. The main treatment priorities are Damage Control Resuscitation (DCR), of which haemorrhage control and blood transfusion are among the most important tenants of DCR. Figure 4.6a illustrates how the casualty is transferred to the helicopter. In Figure 4.6b we can see that the enhanced MERT team delivers blood, keeps the patient warm and performs anaesthesia.

Catastrophic haemorrhage is one of the main reasons of death even for the soldiers that reach a medical team facility in Role 2 or 3 [107]. At this point a DCS is performed (Role 2). DCS is meant to be utilised as a measure that saves lives and prevent metabolic acidosis, hypothermia, and coagulopathy. A multi-disciplinary group of individuals is required: nurses, surgeons, blood bank personnel and others. The approach would provide a limited surgical intervention to control both haemorrhage and contamination. Here, the clinician needs to manage the limited resources and prioritise the evacuation. For instance, when limited blood products are available, and many casualties arrive at the same time, the clinician decides whether to split the blood products among the casualties or try to save those who are more likely to survive. In Role 3 the decisions are related with how to treat the

Figure 4.3: Role 1 facility and medical personnel

This image was provided by Major Max Mardsen (second from the left).

Figure 4.4: Role 2 environment

This image was downloaded from `http://www.marcodilauro.com/`.

problem. At the beginning, the clinical team examines the casualty (Figure 4.5a) and then decides whether to wait for more results, such as CT scan results, or go straight to theatre for a definitive repair (Figure 4.5b).

4.2 Medical Collaborators

This section describes the medical collaborations that provided clinical knowledge and data used in the combat case study.

(a) Resuscitation room (b) Inside theatre

Figure 4.5: Role 3 environment

Image (a) was downloaded from `http://www.marcodilauro.com/`.
Image (b) was provided by Major Max Mardsen (found from google images).

4.2.1 Medical Domain Experts

A medical PhD student and research fellow at RLH, Miss Somayyeh Mossadegh (SM), provided clinical knowledge for understanding the case study and developing the decision support model presented in this thesis. Her contribution was also to make systematic literature review and verify clinically the developed model.

A British DMS surgeon and consultant trauma surgeon at RLH, Colonel Nigel Tai (NT), helped us to understand better the environment of combat trauma care. He was also involved on the clinical verification of the developed model. NT was SM's primary research supervisor.

A general British DMS surgeon registrar and research fellow at RLH, Major Max Mardsen (MM) with an addition of expertise on the deployed combat trauma care was involved in various aspects of this thesis.

4.2.2 Royal London Hospital and Royal Centre for Defence Medicine

The case study was done in collaboration with the trauma unit at RLH. RLH is an internationally recognised leader in trauma care and trauma research. The trauma unit is the busiest in the UK treating over 3400 injured patients in a year, a quarter of who were severely injured. All our medical experts were based at RLH.

(a) Transfer to MERT (b) Inside MERT

Figure 4.6: Enhanced MERT

Both images were downloaded from `http://www.marcodilauro.com/`.

Further collaboration was with the Academic Department of Military Surgery and Trauma within RCDM. The primary function of RCDM is to provide medical support to military operational deployments. It also provides secondary and specialist care for members of the armed forces and is a dedicated training centre for defence personnel with a focus on medical research. The RCDM is a tri-service establishment, meaning that there are personnel from all three of the armed services. It is based at the new Queen Elizabeth Hospital in Birmingham, with defence personnel fully integrated with the National Health Service (NHS) staff to treat both military and civilian patients.

Data on all seriously injured casualties treated by British DMS is collected by the deployed Trauma Nurse Co-ordinator and returned to the Joint Theatre Trauma Registry (JTTR) maintained by the Academic Department of Military Emergency Medicine (ADMEM) at the RCDM. A subset of the JTTR dataset was used for developing the CDS BN for this case study. A more detailed description of the dataset is available in Section 4.5.

4.3 Trauma Casualties

This section aims to increase our understanding about the nature of combat casualties. In addition, it explains why improving combat trauma care could greatly impact civilian trauma care.

4.3.1 Understanding Combat Casualties

Lessons learned from past conflicts should not be forgotten and ongoing basic science and translational research is necessary to truly understand and manage complex combat trauma casualties [31]. The value of learning from past experience has led to important lessons learned [87], [7]. Within the past decade, there has been extensive research, both in the UK and the US, to expand the current knowledge and optimise future combat trauma care. The vast majority focuses on casualties that are classified as died of wounds (DOW), [36], [119], [35], [108], [210]. DOW should be limited to those personnel who died because of injuries inflicted by hostile action after reaching a medical treatment facility [40], [229]. Evaluation of deaths at this level has shown significant performance improvement potential [62].

More recently, there is an increased interest in studying casualties that are classified as killed in action (KIA). KIA is the percentage of the casualties dying of hostile action before reaching a medical treatment facility [229]. This relative blind spot is exacerbated by several factors, including a lack of prehospital data, and an incomplete understanding of the tactical circumstances in which the injuries were sustained. Although some injuries are inevitably fatal, such as decapitation, death may be avoidable in some cases. The severity of the casualties can be prevented by particularly personal protective equipment, changes in tactics, improvements in evacuation and prehospital resuscitation.

To sum up, significant advances in casualty care and combat trauma surgery occurred over the past 100 years. Improvements in aeromedical evacuation, surgical techniques, and resuscitation strategies, as well as a better understanding of the physiologic response to injury have led to increased survival despite rising injury severity [31].

4.3.2 Benefits Beyond Combat Trauma Care

In the civilian sector, increased prehospital capability and expertise, as well as rapid transport to surgical and hospital care, have been shown to improve trauma outcomes. Combat scenarios further complicate matters because of the austere environment and the scarcity of resources. Geographical distances and other tactical limitations often prolong evacuation times. These attributes of the battlefield, along with the particular characteristics of combat injuries, significantly differentiate military trauma care from its civilian counterpart [87].

Apart from that, combat injuries differ from those injuries encountered in civilian practice in terms of epidemiology, mechanism of wounding and outcome. According to Champion et al. [40] some factors unique in combat are:

- Higher energy of the injury
- Higher mortality
- Multiple causes of wounding
- Predominance of penetrating and blast injuries
- Persistence of threat in tactical settings
- Austere resource-constrained environment
- Delayed access to definite care

Despite those differences, medical care provided on the battlefield has been long recognised as a platform for learning and for applying lessons learned, both in military and civilian medical systems. While some of the medical advancements of combat trauma care will remain irrelevant to civilian medical systems and vice versa, others offer great opportunities for implementation of lessons learned on the battlefield to civilian medical care [87]. According to the World Health Organisation (WHO) more than five million people die from traumatic injuries per year. Approximately a quarter of the five million deaths from injuries are the result of suicide and homicide, while road traffic injuries account for nearly another quarter. Other main causes of deaths from traumatic injuries are falls, terrorist attacks, and day-to-day criminal violence. As a result, lessons learned from combat trauma care can create potential for many additional lives to be saved in the civilian sector [108], [35].

4.4 Existing Models in Trauma Care

Most models used in trauma care are scoring systems that calculate a score for the situation of a patient using several inputs [228]. The overall utility and validity of trauma scoring is dependent on clinical personnel undertaking comprehensive and accurate data collection, in real time and near-real time. They are not used for decision support, but as a retrospective descriptor of the clinical condition. Scoring systems are based on anatomical or physiological descriptors, or a combination of both. Each group of scoring systems is presented in the following sections.

4.4.1 Anatomical Trauma Scoring Systems

The abbreviated injury scale (AIS) summarises the severity of anatomical injury in different body parts. AIS was introduced by the American Medical Association and the Association for the Advancement of Automotive Medicine in 1971 to provide researchers with a simple numerical method for ranking and comparing injuries by severity, and to standardise the terminology used to describe injuries. It was modified in 1998 and in 2005 to enhance and improve the system. In the 2005 revision, more than 2000 injuries were described and there was an independent military directory, which helped considering differing circumstances under which military injuries occur. It assigns a six-figure description code together with a severity score to individual injuries (penetrating and blunt). The code facilitates electronic entry and retrieval of data. The severity score ranges from 1 to 6 and is nonlinear. The maximum AIS, which is the highest single AIS of a patient with multiple injuries, has been used as a predictor of outcome and is a good discriminator for survival [171]. Trained and experienced staff are required to code data and to perform scoring; minimising inter-observer variation is important, and a quality control system is needed [173].

The injury severity score (ISS) summarises the severity of all injuries combined by using AIS scores [11], [12]. All injuries are coded using the AIS injury descriptors and divided into six body regions. The highest severity score from each of the three most seriously injured regions is taken and squared. The sum of the three squares is the ISS, which has a range of 1–75. A score of 75 is incompatible with life, and therefore any patient with an AIS 6 injury in any one region is awarded a total score of 75. An ISS greater than 15 signifies major trauma, as a score of 16 is associated with a mortality rate of 10%. ISS is an internationally accepted tool to assist in predicting probability of survival and to identify unexpected outcomes [246]. However, the ISS cannot be used in isolation as it underestimates multiple injuries in the same body region. For example, only one amputated limb will be scored in the event of multiple amputations. In addition, since the ISS is based on the AIS, it is also a nonlinear measure. The non-linearity is a disadvantage as a patient with an isolated AIS 5 injury is more likely to die than a patient with both an AIS 4 injury and an AIS 3 injury. However, both patients will have an ISS of 25. Finally, an equally important disadvantage is that it takes no account of the tactical military situation [106].

The new injury severity score (NISS) indicates the severity of injuries using the highest

AIS regardless of the body region [203]. One of the main criticisms of ISS is that it fails to consider multiple serious injuries in one body region. This is a serious disadvantage in a military population, where multiple ballistic wounds commonly occur in the same body region causing distinct, significant injuries. A second serious injury in the same body region would be ignored when calculating ISS, in favour of a less serious injury in a different body region, potentially underestimating mortality. This led to the development NISS. NISS is calculated from the sum of the squares of the three highest AIS injury codes, irrespective of their body region. This ability to account for multiple serious injuries in one region reduces the underestimation of mortality seen in ISS.

4.4.2 Physiological Trauma Scoring Systems

The revised trauma score (RTS) is one of the earliest scoring systems about patient physiology [42], [43]. It was originally developed as a triage tool that assigns patients to trauma care if they score less than a predefined threshold value. However, RTS has been mainly used to predict mortality as it is found to be correlated with the rate of survival. RTS is based on three parameters: respiratory rate, systolic blood pressure and Glasgow coma scale (GCS). Each parameter scores 0–4 points, and this figure is then multiplied by a weighting factor. The resulting values are added to give a score of 0 to 7.8408. The weighting factor allows the revised trauma score (RTS) to take account of severe head injuries without systemic injury, and be a more reliable indicator of outcome. The first recorded value for each parameter after arrival at hospital is used to ensure consistency in recording, although it has been shown that field values for GCS are predictive of arrival values and make little difference to the accuracy of the RTS. Several studies indicate that RTS is overly simple and lacks important factors, such as those about anatomy, for predicting mortality [83].

4.4.3 Combined Trauma Scoring Systems

The trauma injury severity score (TRISS) estimates the probability of survival through a combination of the RTS (probability related to physiology on first presentation at hospital) and ISS (probability related to anatomical injury) [30]. Weighting coefficients are used for blunt and penetrating trauma, and a logarithm is applied. Different study groups may use their own coefficients to take account of the characteristics of the trauma seen in their populations. By convention, patients with a probability of survival (Ps) of less than 50% who survive are ‘unexpected survivors’ and those with a Ps greater than 50% that die are

'unexpected deaths'. TRISS is not valid for children under the age of 12 years. TRISS incorporates ISS and its limitations and, therefore, will overestimate Ps for patients with multiple injuries in the same isolated body region. It must be stressed that the Ps is a mathematical expression of the probability of survival, and not an absolute statement of the patient's likely outcome. One in four patients with Ps 75% will still be expected to die. While these cases may be highlighted for audit to identify lessons to be learned, conclusions about system performance should not be drawn from single patients. TRISS can usefully compare performance between trauma systems or against a national standard, where the limitations of the model apply consistently.

The severity characterisation of trauma (ASCOT) is a more recent system, first described in 1990 [41]. It has proved more reliable than TRISS in predicting outcome in both blunt and penetrating trauma as it takes account of more than one injury in a single body region. ASCOT also uses the individual components of the RTS and a more detailed age classification, but this makes it a more complicated calculation. ASCOT has not replaced TRISS because the improvement in performance is small and the increased difficulty in calculation outweighs the benefit.

4.4.4 Limitations of the Existing Scoring Systems

The trauma scoring systems that are based on anatomical descriptors do not consider physiological descriptors and vice versa. Young, fit soldiers have compensatory physiological mechanisms that allow them to maintain near normal vital signs, despite severe anatomical injuries. In contrast, many elderly trauma victims will have markedly disordered physiology prior to their injuries and may be taking medications that affect the body's response to trauma [228].

Combined systems that use both physiological and anatomical descriptors (TRISS, ASCOT) are the most reliable, but are more complicated to apply. In addition, their calculations are both based on coefficients for either blunt or penetrating injuries. There is currently no coefficient for explosive injury and given that this is the most common injury mechanism in the battlefield, it can be considered as a significant limitation of the methods [210].

Another strong limitation of all the described scoring systems is that they cannot be calculated when some necessary elements are missing; a frequent scenario in many medical problems. These scoring systems can be calculated only once and normally when the patient reaches the hospital. As a result, neither pre-hospital scores nor multiple scores that show the progress of the patient's condition are available. Physiological parameters that change in response to treatments and sentinel events during the patient's care cannot be captured by the existing trauma scoring methods.

To sum up, these trauma scoring systems are relatively simple mathematical models to quantify the complex human response to injury. They can only give an assessment of the overall condition of the patient at a specific time point. They can be calculated once and only when all the necessary information is available. As described in Section 4.1.2 several decisions are taken in successive stages of the soldier's care. As a result, a static score, which does not capture the progress of the patient's condition, cannot support the evolving process of clinical decision making. The existing trauma scoring systems may be useful as a retrospective indicator of the severity of the injury, but they do not present the complete causal story of the clinical pathways and they cannot assist clinical decision making in successive stages of the soldier's care (see Section 2.6 and Chapter 5). Finally, they cannot explain where the estimated score came from (see Section 3.3.2 and Chapter 7) and they cannot be used for more sophisticated techniques such as interventional or counterfactual reasoning (see Section 2.5 and Chapter 6).

4.5 Combat Injury Data

This section describes the data used for the combat trauma care case study. Those datasets were used for developing and validating the BN model presented in Chapter 5.

4.5.1 JTTR Dataset

The UK Military JTTR is an electronic database of prospectively gathered information on all casualties collected by trained trauma nurse coordinators working both in deployed medical facilities in Iraq and Afghanistan and in the RCDM in Birmingham. All fatalities and traumatically injured casualties that trigger a 'trauma alert' on presentation to deployed UK medical facilities or subsequently require return to the UK following injury are included.

Returns are either electronic, where deployed IT systems allow, or more frequently in hard copies (Appendix A). The database is managed by the clinical information and exploitation team and administered by the UK defence statistics and its accuracy is entirely dependent on the quality of data collected by the trauma team scribe and the deployed trauma nurse co-ordinator.

JTTR is part of the Major Trauma Audit for Clinical Effectiveness (MACE) and it was developed by military medical leaders to provide a systematic and integrated approach to battlefield care [246]. Its main purpose is to capture vital injury information for performance evaluation and improvement as well as combat injury epidemiology and surveillance. JTTR includes 6797 cases, from 2009 to 2013. A shown in Figure 4.7, 83% of the casualties are due to hostile action. From those cases, 81% are wounded in action (WIA), 13% KIA and 6% DOW. Table 4.1 summarises the available information in the JTTR database.

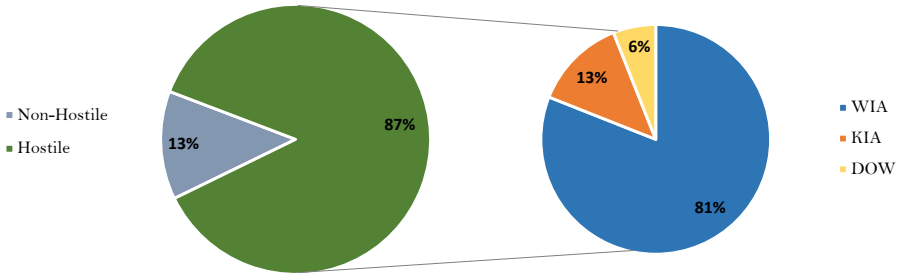

Figure 4.7: Distribution of JTTR dataset

4.5.2 MERT Dataset

The MERT database is an electronic record of patients treated by the British MERT (physician led helicopter). Only patients delivered to UK medical facilities are included. Originally, MERT was intended to be part of the MACE dataset as JTTR. However, it became separate. The MERT dataset contains the same data as JTTR (Table 4.1), but the method of collection differs. It is done using the clinical patient record form filled in by the MERT doctors during en route care (APPENDIX B). It is then transcribed into an electronic format by members of the Clinical Exploitation team at RCDM. MERT includes almost 4000 cases, from 2009 to 2013.

Data Section	Available Information
Patient Characteristics	Age, Gender and Service
Injury Characteristics	Intention (hostile or non-hostile), Mechanism and Energy of the Injury, detailed Injury Description, Regions of the injury and Injury Severity Scores: ISS, NISS, RTS, TRISS, ASCOT
Physiological observations	Systolic Blood Pressure, Diastolic Blood Pressure, Respiratory Rate, Oxygen Saturation, Body Temperature, Heart Rate, Glasgow come score and white cell counts (different observations where available in each role of care, e.g Heart Rate in Role 1, Heart Rate in Role 2 etc.)
Timings	Time of Injury, minutes to Role 1, minutes to the Emergency Department and minutes to first Operation
Interventions	Treatments performed in each Role, Drug, Fluids and Blood Products given
Outcome Details	Survival Outcome, Abbreviation and Force Provider

Table 4.1: Available Information in the JTTR database

4.5.3 Data Characteristics

Because of the unique combat environment, the information is usually in hard copies and the data are typed in at a later stage. As a result, few typing errors exist (e.g. the body temperature is 374 degrees Celsius instead of 37.4). In addition, many non-captured information is replaced by a 0. This is extremely problematic for the physiological variables, as there is confusion between the 0s that mean non-captured and those that indicate the real recorded variable. Apart from the misuse of the 0 value, many variables have a lot of missing values. This is especially true in the pre-hospital setting (Role 1), where the primary aim is to evacuate the soldier as soon as possible and the time for data capturing is limited.

The information captured can be either static or dynamic. Static information is captured once, such as the mechanism of injury, the trauma score, and others. Dynamic information

is captured more than once in regular or irregular time intervals, such as the physiological signs. For some of the static variables it is not clear when they have been captured or calculated. Finally, the information in both databases is not always in the appropriate format and extra processing needs to be done. Figure 4.8 shows a real example. The first box illustrates how a note is captured by a deployed trauma nurse co-ordinator. The second box presents how the hand-written note is saved in the JTTR database. The third box shows how the model understands the information. This is a simple example. However, some model variables may be based on more than one JTTR entries. A more detailed description of how all these factors have been treated in the case study can be found in Chapter 5.

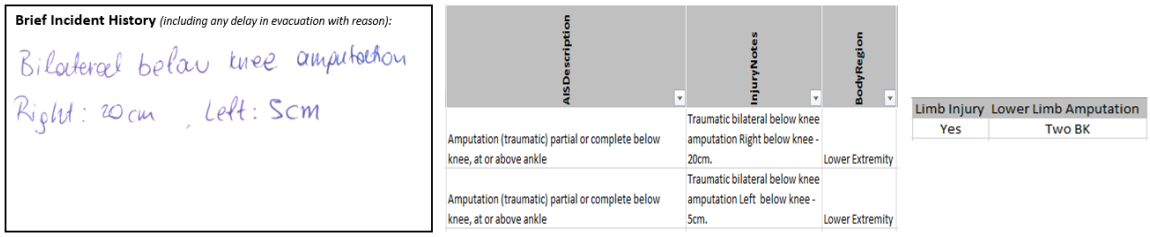

Figure 4.8: Process of translating a clinical note to a model entry

4.6 Mortality and Morbidity Review Meetings

Mortality and morbidity review meetings are an important healthcare governance component in British DMS [246] and they are considered as the bed-rock of quality improvement in trauma care [63]. The main aim of these meetings is to measure the performance of UK deployed clinical services, such as assessment, treatment and evacuation of service personnel, and provide useful feedback [228]. DMS mortality and morbidity review meetings are conducted two or three times a year to provide senior multidisciplinary review of deaths in the intervening periods [229]. During busy periods, in terms of casualty burden, mortality and morbidity review meetings run more regularly (every 2-3 months). Those meetings are overseen by the Defence Professor of Emergency Medicine and ADMEM. Representatives from the defence science and technology laboratory DSTL review the protective equipment. Usually the trauma nurse co-ordinator, who had attended the autopsy, will also be present alongside the home office pathologist. The aim of these meetings is to identify preventable and surgical salvageable casualties to inform the defence surgical doctrine and guide resource utilisation, training and research [229], [246].

All operational deaths are reviewed at the mortality and morbidity review meetings whether the death occurred on the ground, during evacuation by the MERT, at the deployed hospital (Role 3) or following repatriation to the UK (Role 4). For each case, the medical and military context are defined using clinical notes, post-mortem and incident reports, and they are presented to the mortality review panel as shown in Figure 4.9. The top left box gives some general details about the incidence and the main causes of death. In this box there are also two trauma scoring systems: ISS and NISS. As described in Section 4.4, both scoring systems are simple models that are calculated either in Role 3 or Role 4, when all the necessary information is available, and they give a sign of the injury severity [228]. They are based only on anatomical descriptors, so they cannot really represent clinical practice. The top right box describes all the major injuries. In the bottom left box, all the medical treatments/ interventions performed at different stages of the soldier's care are explained. Finally, identified issues are included in the bottom right box.

Initials, Case Reference Number **Incident:** MOI, Date, Time **Cause of death:** Multi organ failure Blast injuries caused by explosion **ISS: 75** **NISS: 75** **DOW**	**Major Injuries:** - Thoracic and lower body fragmentation wounds - Axilla and artery and vein injuries (operated on) - Left lung pulmonary lacerations x 3 - Gastric perforation - Open tibia fracture - Left kidney laceration - Ischemia liver
Medical Interventions: **Ground:** No information **MERT:** Findings and Interventions **Role 3:** Theatre – Laparotomy, Thoracotomy, Graft of axilla artery and vein, scrotal and lower leg debridement. CT scan: Key findings **CCAST:** No information **Role 4:** Died on "date" shortly after arriving at R4. **PRBC: 3 FFP: 3**	**Issues Identified:** **Clinical:** Nil **Other:** Nil **Force Protection:** Nil

Figure 4.9: Notes for a combat trauma fatality presented in a DMS mortality and morbidity review meeting

Following the review of the clinical and military notes (Figure 4.9) by the members of the review panel, a judgement of the outcome takes place from two viewpoints: preventability and salvageability. The preventability of death refers to how likely is that intervention was possible, given the tactical circumstances and resources. A 3-point scale is used as an answer; preventable (P1), possibly preventable (P2), and unpreventable (P3). When judging the salvageability of death, the review panel examines the likelihood of attempting interventions and what would have been the outcome if interventions had been attempted. A 4-point scale is used as an answer [229]; salvageable (S1): intervention would likely have influenced survival ($P(Survival) > 95\%$), potentially salvageable (S2): intervention would have been attempted and may have influenced survival ($5\% \leq P(Survival) \leq 95\%$), possibly salvageable (S3): intervention would have been attempted but with a high probability of mortality ($P(Survival) < 5\%$), non-salvageable (S4): intervention would not have led to survival ($P(Survival) = 0$). For cases classified as S1 – S3, further counterfactual questions can be asked from any member of the review panel regarding tactical, equipment and clinical factors. For instance, hypothetical question such as 'If we had performed a thoracostomy, what is the likelihood that the soldier would have survived?' are usually asked during the DMS mortality and morbidity review meetings. An objective way to answer these counterfactual questions is proposed in Chapter 6.

4.7 Conclusion

In successive roles of soldier's care, clinicians should take several decisions based on the patient's condition and the available capabilities. Thus, having a model that can capture the rapid progress of the patient's condition is very important. Different trauma scoring systems have been developed to summarise the patient's condition (see Section 4.4). The main problems of the existing scoring systems are: (1) the scores cannot be estimated or they can be less reliable when any necessary information is missing, (2) they are static, meaning that they cannot capture the progress of the patient's condition, (3) important elements in combat trauma care such as: evacuation times, treatments, sentinel events, and blast injuries are missing, (4) more complicated reasoning techniques cannot be performed and (5) they are intended to be used retrospectively.

These limitations demonstrate the need of developing a novel methodology for creating a model that has the following characteristics: (1) capture the rapid patient's progress, (2)

capture the dynamic process of clinical decision making, and (3) account for all the data characteristics as described in Section 4.5.3.

In Chapter 5, we propose a method for building a CDS BN that captures the progression of an acute condition and gives predictions in successive stages of care. The proposed BN can reason in a manner consistent with clinical knowledge without being limited by the observed data. The combat trauma care described in the chapter is used as a case study.

Mortality and morbidity review meetings have been used as a quality assurance to review combat trauma care. Currently, the review panel judges the outcome from a preventability and salvageability point of view. Their judgement is subjective, and it is based on the clinical and military notes and the available scoring systems. However, the existing scoring systems can only describe the injury severity. As a result, a more objective tool that consider treatments and their effect on soldier's salvageability could add an additional assurance to the current practice.

In Chapter 6, we propose an alternative use of the model developed in Chapter 5. Particularly, we explain how we can use the developed model, alongside the current practice, as a healthcare governance tool to answer counterfactual questions about the effect of treatment decisions, other than those occurred to assist the DMS mortality and morbidity review meetings.

Chapter 5

Developing a Progressive Bayesian Network for Modelling the Evolution of an Acute Medical Condition and the Dynamics of Clinical Decision Making

Developing models that accurately capture the way clinicians gather information and make decisions during the stages of a patient's care is challenging. The modelling problem is especially difficult for acute conditions that evolve rapidly over a short timescale. In Section 2.6, we presented various time-based BNs that have been developed to address this challenge, but they make assumptions that are rarely true in acute medical conditions (see Section 3.2). In this chapter, we present a methodology for developing a progressive BN that models the rapidly evolving progress of an acute condition, and captures the way clinicians gather information and make decisions in successive stages of care. To overcome the typical lack of data for this type of problem, we use a combination of expert knowledge and available data to produce a causally coherent BN. The method is illustrated throughout using a comprehensive case study on predicting the mortality risk to combat trauma casualties in two successive stages of the soldier's care. In Chapter 4, we described the context of combat trauma care, where the limitations of the existing trauma models and the characteristics of the datasets highlight the need for a new modelling technique. The proposed model could be used to support clinical decision making in successive stages of care.

5.1 Introduction

One of the major challenges in developing useful clinical decision support systems for specific medical conditions is to model the dynamic process of decision making as the condition progresses. Unlike 'chronic' conditions, such as diabetes, which develop over a long timescale, an 'acute' medical condition is one that develops suddenly over a short timescale and in which, symptoms and treatment capabilities can vary greatly and rapidly at each stage of the patient's care. Consider the example of a person suffering trauma, such as a severe head injury from a car accident. The symptoms, diagnostic tests and treatment strategies vary based on whether the patient is treated in an ambulance, in the ED, or in the ICU. Moreover, the information on which the decisions are based, especially at the beginning, might be limited. For instance, in the car accident example, the information at the beginning might be limited to the injury description and physiology. In the ICU, more data about blood results, operation's response, fluid and drugs given will be available.

Over the years, many researchers have expressed the need to represent the dynamic nature of clinical decision making [5], [146], [152], [258], [10], [3], [120]. As explained in Section 2.6, many time-based BNs have been proposed. Despite their benefits, modelling an acute medical condition remains challenging (see Section 3.2). In this chapter, we propose a practical methodology for doing so. The methodology captures the way clinicians gather information and make decisions in successive stages of care. Crucially, by exploiting expert knowledge, the methodology is not limited by the available data. The method can generate several predictions in successive stages using a progressive BN. The term 'progressive' refers to the evolving non-stationary structure of the model which, at each stage, is an extension of the previous stage. We use the term 'stage' and not time slice as we provide predictions in successive stages of the patient's care. The time interval between each stage is irregular and follows clinicians' timeline and not data availability. To illustrate and validate the methodology we use a clinical case study on predicting the mortality risk to combat casualties in the prehospital setting.

The chapter is organised as follows: in Section 5.2 we briefly introduce the characteristics and the development process of a progressive BN. We illustrate our methodology using a case study, which is described in the same section. The way to define the model's variables is described in Section 5.3. The process of developing the BN structure is explained in

Section 5.4. In Sections 5.5 and 5.6 we describe the process of parameter learning and elicitation, and the validation of the model's performance, respectively. Finally, a discussion is provided in Section 5.7.

5.2 Developing a Progressive BN for Acute Medical Conditions

This section describes the main characteristics of a progressive BN, as well as its development process. In addition, it introduces the case study used for illustrating the methodology.

5.2.1 Characteristics and Development

A progressive BN is a non-stationary BN that can be used in irregular stages of care. Irregular means that for a specific case the time interval between stages 1 and 2 is different from the time interval between stages 2 and 3, but also that these time intervals are allowed to vary among different cases. The term 'non-stationarity', as explained in section 2.6.3, indicates that the structure and/ or parameters of the model may vary at each stage. An example of a progressive non-stationary BN is shown in Figure 5.1. As we can see, the structure does not remain the same in the three stages, and variables that are included in one stage might not be part of the following stage and vice-versa. Two important differences with the non-stationary time-based BNs presented in section 2.6.3 are: (1) the variables included in each stage are not restricted to the observed data, and (2) the set of variables included in each stage are not restricted to be the same, allowing only the relationships to vary among them. This evolving structure, which at each stage is an extension of the previous one, justifies also the term 'progressive'.

Having a progressive BN helps us to capture the progress of the condition, and the progressive way clinicians gather information and take decisions in successive stages of care. Apart from the progressive structure, the reasoning process is progressive as well. Using the example shown in Figure 5.1, imagine that we want to predict the likelihood of $D = True$. Suppose that we are in stage 1 and only $A = True$ is observed, then the probability in question becomes $P(D_1 = True|A = True) =$? When we reason in stage 1, the part of the model that covers stage 1 is used (BN 1), while the part of the BN that covers stages 2 and 3 is redundant. When for the same case, the same prediction is needed in stage 2 and

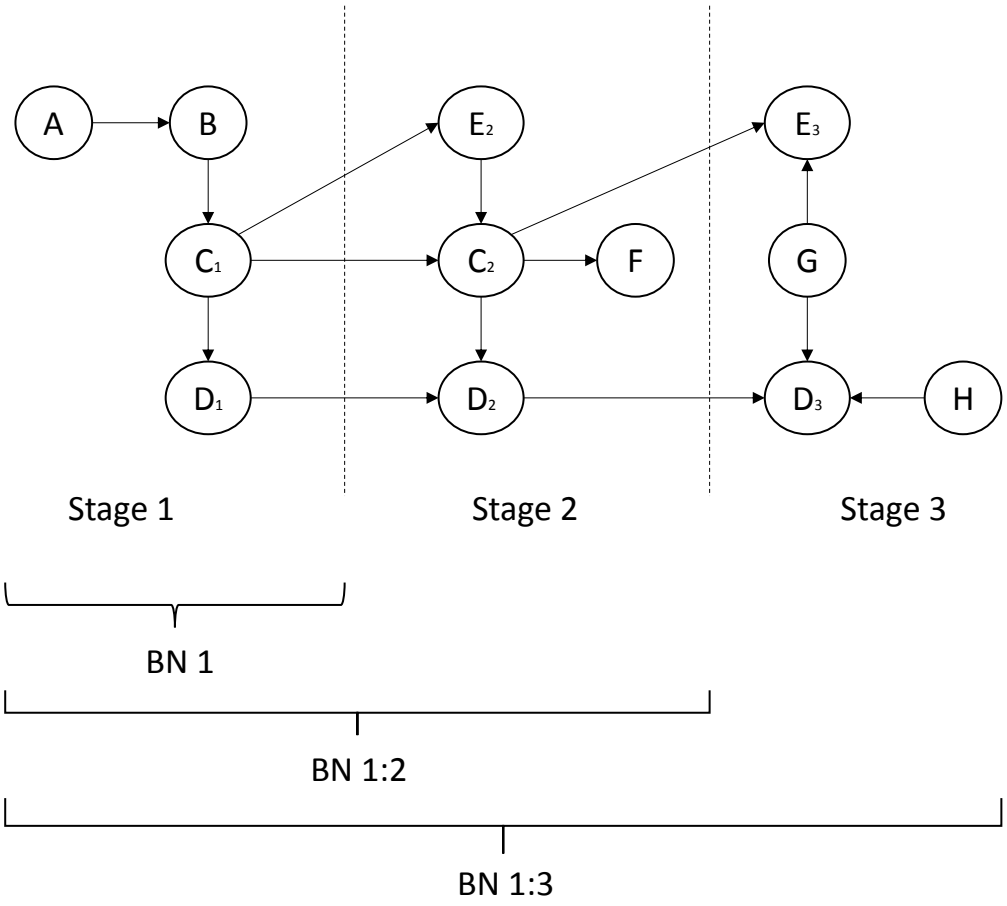

Figure 5.1: A progressive non-stationary BN

only $E_2 = False$ and $D_1 = False$ are observed, then the probability in question becomes $P(D_2 = True|A = True, E_2 = False, D_1 = False) =$? All the evidence that were observed in stage 1, as well as the new evidence observed in stage 2 are instantiated. It is important to highlight that when we are in a specific stage, the outcome variable in all the previous stages is known. Therefore, D_1 becomes an evidence in stage 2. When we reason in stage 2, the part of the model that covers stages 1 and 2 is used (BN 1:2), while the part of the BN that covers stage 3 is redundant. Only reasoning in stage 3 makes use of the complete model (BN 1:3). For generalisation, imagine that we have a progressive BN that covers the evolution of an acute condition and the dynamics of the clinical decision making process in n stages of care. When we want a prediction in stage i, we make use of the BN 1:i. In addition, the outcome in stages $i-1$ is known and it becomes an evidence in stage i.

The challenges in developing a progressive BN will be described using the four widely acceptable components that follow:

1. Identify model variables

2. Develop model structure

3. Learn and/or elicit model parameters

4. Validate model performance

In the first component, we will explain how we can elicit expert knowledge to understand the progress of an acute condition, the increasing information that is available and the dynamic process of clinical decision making. In addition, we will explain how the elicited knowledge can be categorised into generic and specific group of variables to facilitate the development of the BN structure. In the second component, we will present several ways to incrementally translate the elicited knowledge into a progressive BN. In the third component, we will describe how we can learn and/or elicit the model parameters from data or experts, respectively. Moreover, we will describe how the parameter learning can be done progressively when an unequal number of patients is available at each stage of care. Finally, in the last component we will explain how we can progressively validate the performance of a progressive BN. The flow from one component to the other follows the spiral model proposed by Laskey and Mahoney, where the lessons learned at each component are used to plan the next components of the development (more details about the spiral method in section 2.3.1). The described challenges related to each of the four components will be explained in detail in the following sections.

5.2.2 Acute Condition Case Study

To avoid completely abstract concepts, we illustrate the method throughout using the case study on combat trauma care in which we want to capture the rapidly evolving condition of an injured soldier and the clinical decision-making process. After a trauma injury in combat, the soldier's condition evolves rapidly in a very short timescale and several critical decisions should be taken in successive stages of the soldier's care based on uncertain and limited information (see Section 4.1). Most combat deaths occur before reaching a medical treatment facility; therefore, prehospital care is of paramount importance [20], [117]. The sparse and uncertain information, and the acute condition of the soldier, make the process of clinical decision making in the prehospital setting very challenging. Although there are existing models for trauma care, they are not used in the prehospital environment (see Section 4.4). In addition, their purpose is to describe the severity of the injury at a specific time point and they cannot capture the progress of the soldier's condition. Therefore, the

aim of the case study is to predict the mortality risk of the soldier given the observed symptoms, injury details and the effect of the initial lifesaving treatments in the highly uncertain prehospital setting. The prediction could help clinical decision making in several ways, such as: triaging the patient, managing the evacuation time, or assisting future treatment strategies. To achieve our aim, we use a progressive BN in two successive stages of care: field care, and emergency care (care given during the evacuation). The developed BN that models the field care is the first part of the model; we will refer to it as the BN 1. The BN that models also the emergency care is an extension of the BN 1, and we will refer to it as the BN 1:2 (similar to the abstract structure shown in Figure 5.1). In addition, throughout this chapter we will refer to the field care as stage 1 and the emergency care as stage 2. The proposed modelling approach can be extended to more than two stages of care.

5.3 Identifying Model Variables

Defining the variables that should be included in the BN is a difficult and time-consuming task. This task is even more challenging when developing complex progressive BNs that capture an evolving condition and the dynamic process of clinical decision making in successive stages of care. In this section, we propose a practical way to identify the variables included at each stage.

5.3.1 Expert Knowledge Elicitation

As mentioned before, an acute condition is a sudden condition and the available information, especially at the beginning of the patient's care, might be limited. Therefore, including in the model only variables that are available in the data might be too restricted. In addition, even in cases when rich data is available, it might still not be complete enough to be used as the only source of evidence. In many medical BNs, latent variables are modelled [282]. These variables are important and should be included in the model, but they are not available in the data either because they cannot be measured or because they were considered as irrelevant for clinical use. Domain experts can help us find the necessary information as they may have access to information that is not machine-readable or even available in the data.

When the model's variables are captured from domain experts, it is very important to know

how to communicate with the experts and extract the necessary information. Eliciting expert knowledge is not an easy task. In this section, we propose a three-step process to facilitate expert knowledge elicitation:

1. *Background knowledge capture*: capture the necessary background knowledge using semi-structured interviews with broad-open and probing questions.

2. *First review*: review the main parts of the elicited knowledge using simple BN fragments.

3. *Second review*: review the extra details of the elicited knowledge base using conditional scenarios.

Using the case study on combat trauma care, we describe how each step of the expert knowledge elicitation process can be done.

Background Knowledge Capture For facilitating the knowledge elicitation, we propose to focus the process on the following topics:

1. *Problem context*: clarify the problem context and how the model is intended to improve the current situation. Questions such as 'What medical problem do you want to investigate?', and 'How you hope the model to change clinical practice?' can be useful.

2. *Condition progress*: clarify the characteristics and the evolvement of the medical condition in question along the successive stages of care.

3. *Decision making process*: clarify the decisions and actions taken at each stage of care.

Before asking specific questions, it is best to let clinicians explain these three topics with their own words without guiding the conversation. This stage helps clinicians to explain their own practice and experience, and the model expert to obtain a general understanding. It is important after the first conversation with clinicians to divide the problem into smaller sub-problems. The method of divide-and-conquer it is useful not only for developing the BN structure (see section 2.3.1), but also for eliciting expert knowledge. When building a progressive BN that model different stages of care, an obvious way to divide the problem is by focusing on each stage of care separately. The next step of the elicitation process is

to ask specific questions for each previously defined sub-problem. During that stage, the model expert should guide the conversation and ask specific questions about variables that are key to medical BNs, such as risk factors, symptoms, signs, diagnostic tests, and interventions.

In this case study, two experienced clinicians, SM and NT (see Section 4.2.1), helped us to understand the knowledge needed to build the BN. First, we asked them few broad-open questions to get an understanding of the three topics described above. During our first meeting we clarified the stages of care from the point of wounding to the soldier's arrival in Birmingham. These stages of care were used as an initial division of the problem. In our particular clinical context, we noticed that every decision taken by clinicians at each stage of care was highly related to the soldier's type of injury. The injury was the trigger of each care pathway. This was the first clinical event that happened and set off a sequence of clinical disorders that can lead to the outcome, which in this case study was death. We had five triggers representing five major trauma injuries; chest, abdominal, pelvic, limb and head injury. These five triggers were used to divide the problem further. Specific questions were asked for each trigger. As opposed to Van Gerven et al, who propose asking questions about the immediate causes of the condition in question [265], we found more useful to start the elicitation process from the triggers. This helped us to understand better the sequence of events from the triggers to the outcome. The questions asked were about key variables of medical BNs like effects/symptoms, diagnostic tests, interventions and causes. For instance, suppose that we wanted to explore the knowledge about a limb injury in stage 1, then the following questions were asked:

1. What are the observed symptoms of a limb injury during stage 1?
2. What are the physiological effects of a limb injury appeared during stage 1?
3. What are the available diagnostic tests for a limb injury during stage 1?
4. What are the available interventions for a limb injury during stage 1?
5. What are the causes of a limb injury during stage 1?
6. How can a limb injury lead to death during stage 1?

As we had divided our problem into 5 sub-problems related to the 5 main triggers, similar questions were asked for each trigger at each stage of the patient's care. As well as facil-

itating the elicitation process, focusing on each trigger separately helped us to understand better how each trigger works. In addition, by asking the same questions in each stage, we could identify whether a variable appears only once, or it is repeated in more stages. A second interview was conducted a week later during which we asked clinicians to review their answers presented as bullet points. This step gave clinicians the opportunity to correct their answers or add anything missed during the initial interview.

First Review The second stage of the expert knowledge elicitation is to review the main cause-effect relationships captured during the initial interviews. In particular, we review their answers in questions 4 and 6 as explained in the above section. We focus the review only on these two questions as they cover two of the most important components of the medical problem: (1) the causes of the condition in question (similarly with the process proposed in [265]), and (2) the decisions/ actions taken at each stage of care. It is always easier to review causal relationships graphically. Thus, their answers can be translated into simple BN fragments modelling the main cause-effect relationships from the trigger to the medical condition in question.

Two of the BN fragments used in our case study are shown in Figures 5.2 and 5.3 illustrating the main causes of death when the soldier suffers from a limb and a chest injury, respectively. Clinicians found that step very helpful as they found these graphs easy to understand and to check their answers. In addition, they liked that we kept the process as simple as possible by presenting separate graphs for each trigger, combining all stages of care.

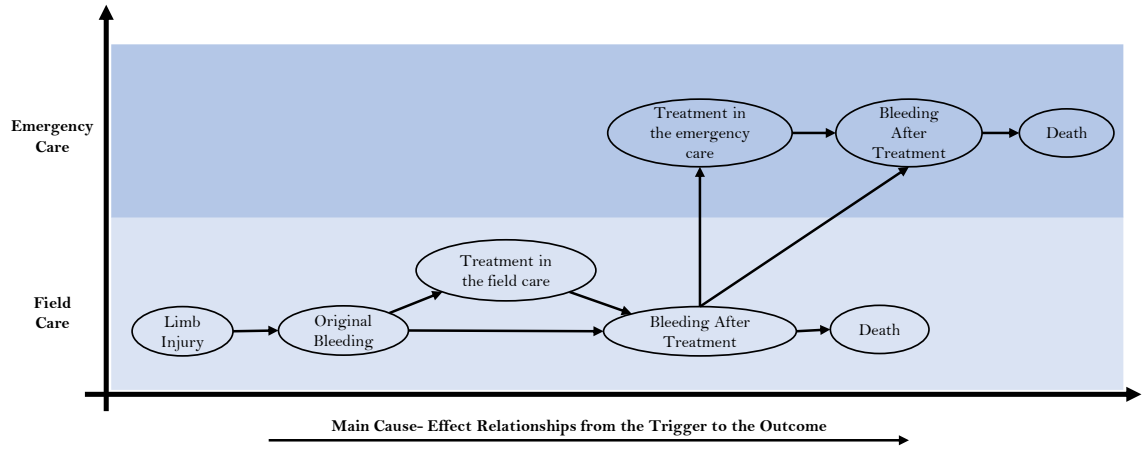

Figure 5.2: Cause-effect relationships related to limb injury

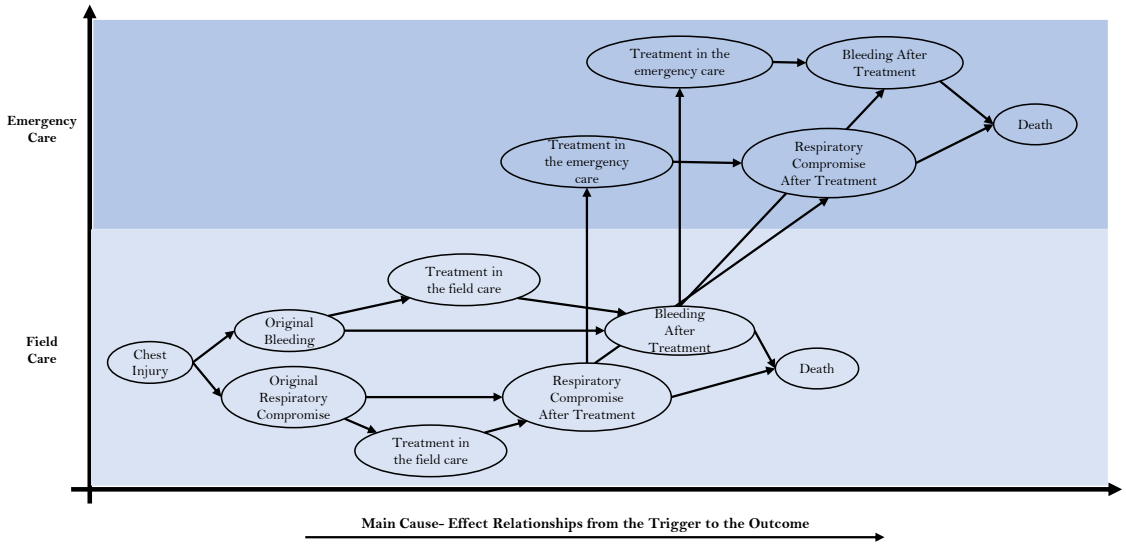

Figure 5.3: Cause-effect relationships related to chest injury

Second Review Finally, the last stage of the expert knowledge elicitation is an additional review. This step is done after an initial BN structure is developed (more details on how to develop the BN structure in section 5.4). In this stage, we review all the variables captured during the initial interview using conditional questions. Each conditional question is related to a conditional dependency captured in the model.

In this case study for instance, clinicians told us during the initial interview that when a soldier has a respiratory compromise, his respiratory rate (RR) is high and his oxygen saturation is low. A BN fragment that captures this information is shown in Figure 5.4. A conditional question asked was: 'If a soldier does not have a respiratory compromise can he still have a high RR and a low oxygen saturation?'. Their answer was yes, because of extensive bleeding in any other body part. This information was not captured in the previous stages. So, based on this third stage, the updated BN structure is shown in Figure 5.5. This final stage had a great impact on the elicitation process as it helped clinicians to think about their answers from another perspective.

Another approach, not followed in this case study, that might be useful when reviewing the elicited variables is to use real clinical scenarios. Looking at some real cases we can verify whether the information collected by clinicians is also captured in our model.

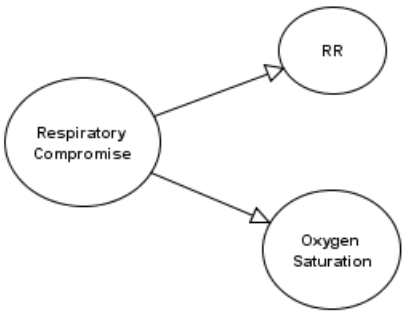

Figure 5.4: Initial BN fragment developed based on the first two stages of expert knowledge elicitation

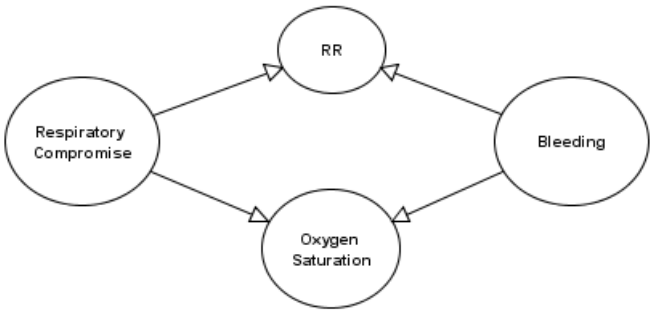

Figure 5.5: Updated BN fragment developed based on all the three stages of expert knowledge elicitation

5.3.2 Variable Categorisation

When we build a BN with a structure that is based primarily on expert knowledge, organising the elicited knowledge into specific categories can be very helpful. When we develop a progressive BN that models several stages of care, it is important to divide the elicited knowledge into two general categories that represent the dynamic nature of the variable, such as:

1. *Persistent*: a variable that is present in more than one stages of the patient's care
2. *Fixed*: a variable that is present in a specific stage of the patient's care

A persistent variable is one that is repeated in more than one stages, while a fixed variable is a static variable that is appeared only once in the progressive BN. This initial categorisation is useful to identify which variables should be included in each stage. Next, the same variables must be grouped further into more specific categories that describe the variable type, the role each variable plays in the BN, such as:

1. *Intervention*: a variable that represents a medical intervention

	Fixed Variables	Persistent Variables
Interventional Variables	Yes	Yes
Transition time Variables	Yes	No
Target Variables	No	Yes
Other Variables	Yes	Yes

Table 5.1: Relationships between the categories of variables

2. *Transition time*: a variable that represents the time needed from one stage of care to another

3. *Target*: the outcome in question

4. *Other*: remaining variables such as symptoms, diagnostic tests, demographics etc.

An intervention is used as a unique variable category, as clinical decisions are an important part of the proposed model. Following Van Gerven et al., we distinguish two types of intervention: (1) regular interventions and (2) treatments [265]. Regular interventions are interventions that clinicians accord almost always for prophylactic reasons. For example, when an injured patient arrives in the hospital, doctors immediately give him fluids for preventing coagulopathy. As a result, a regular intervention can only be a parent node, as it is not triggered by anything else. On the other hand, treatments are interventions that are triggered under specific circumstances. For instance, we do not apply a tourniquet unless we have an extensive bleeding on the limb. The way treatments are modelled, trained and used for inference is explained in sections 5.4 and 5.5. In addition, as a progressive BN is used in irregular stages of care, the transition time is chosen as a unique variable to represent the time interval between two successive stages. The target variable helps us to focus the aim of the model. All the other variables, which have the same importance in any medical BN, can be grouped together. However, this is not an absolute requirement, and further specific categories can be used instead. The connection between the described categories is shown in Table 5.1.

In this case study, persistent variables were variables such as blood pressure or heart rate, while the actual injury was a fixed variable. In our model, stages indicated successive places where the patient was treated, and decisions were taken. These decisions were mainly about initial life-saving treatments. The time of the transition from one stage of care to another

varied a lot from case to case and it was captured using the transition time variables. The target variable was the soldier's survival. Taking the limb injury as an example, we show how we organised the elicited knowledge into specific categories in Table 5.2. A complete table of all the variables included in our model is presented in APPENDIX C.

Table 5.2: Organising the elicited knowledge on limb injury

Variable Name	Variable Description	Variable States	Variable Dynamics	Variable Types
MOI	Mechanism of injury	{Penetrating, Blast}	Fixed (Field Care)	Other
Upper Limb	Severity of upper limb injury	{None, Mild, Moderate, Severe}	Fixed (Field Care)	Other
Lower Limb	Severity of lower limb injury	{None, Mild, Moderate, Severe}	Fixed (Field Care)	Other
LB	Long bone fracture	{No, Yes}	Fixed (Field Care)	Other
UL amp	Upper limb amputation related to injury	{No, Yes}	Fixed (Field Care)	Other
LL amp	Lower limb amputation related to injury	{0, 1, 2}	Fixed (Field Care)	Other
Bleeding Limb BT	State of bleeding before treatment	{Mild, Moderate, Severe}	Persistent	Other
Bleeding Limb AT	State of bleeding after treatment	{Mild, Moderate, Severe}	Persistent	Other
O2 Sat	Oxygen saturation	{Normal, Abnormal}	Persistent	Other
RR	Respiratory rate	{Normal, Abnormal}	Persistent	Other
HR	Heart rate	Continuous	Persistent	Other
SBP	Systolic blood pressure	Continuous	Persistent	Other
Splintage	Applying splintage	{No, Yes}	Persistent	Treatment
Tourniquet	Applying tourniquet	{No, Yes}	Fixed (Field Care)	Treatment

Continued on Next Page...

Table 5.2 – Continued

Variable Name	**Variable Description**	**Variable States**	**Variable Dynamics**	**Variable Types**
Time to R1	Transfer time from point of wounding to the field care	$\{< 1$ hour, ≥ 1 hour$\}$	Fixed (Field Care)	Transition Time
Time to Pick Up	Time the soldier to be picked up from the field care by the emergency response team	$\{< 10$ min, ≥ 10 min$\}$	Fixed (Emergency Care)	Transition Time
Death	Event of death	{No, Yes}	Persistent	Target

5.4 BN Structure

When modelling clinical decisions and their effect on the patient's outcome, a BN that captures these causal mechanisms is needed. Relying on the accuracy of the provided knowledge, clinicians can help us to find the necessary information to develop the BN structure, which follows the natural causal processes. Approaches that combine expert knowledge and data can also be used [80]. Purely data-driven approaches, such as constraint-based algorithms and score-based algorithms, can be used for developing the structure of a BN, but they cannot assure a causal structure. In addition, they require a large amount of high quality data, which is not always available in medicine.

So far, we have explained how to elicit the necessary knowledge from experts and how to organise it into specific categories to facilitate the development of the BN structure. A difficult task that remains is how to connect the elicited variables. Asking clinicians to provide the connection between the variables is not appropriate as they often conclude that with the human body you cannot have distinct cause-effect relationships, as everything is connected to everything. Neil et al. proposed a way to facilitate the development of a BN structure using idioms, such as cause-consequence and measurement idioms [186]. As explained in section 2.3, an idiom can be considered as a more meaningful fragment that has associated semantics. The idioms proposed by Neil at al. can be easily extended to medical BNs. For instance, the relationship between a medical condition and a symptom as shown in Figure 5.6 can be considered as the instantiation of the cause-consequence idiom. In addition, a medical measurement idiom may represent the relationship between a medical condition and a diagnostic test, as shown in Figure 5.7.

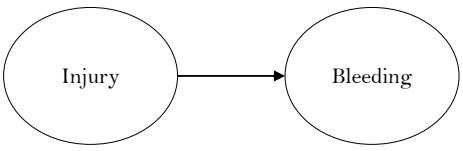

Figure 5.6: Medical example of cause-consequence idiom

As explained before, modelling medical interventions, such as treatments, is very important when we develop medical BNs. However, it is not an easy task and it cannot be represented fully by any of the proposed idioms. As a result, in the list below we propose two medical idioms, the treatment and the treatment follow-up idiom to represent the treatment effect on a fixed and on a persistent variable, respectively.

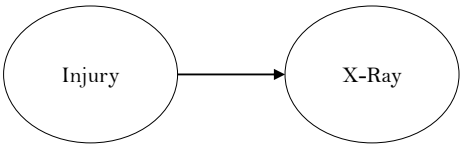

Figure 5.7: Medical example of measurement idiom

1. *Treatment idiom*: this idiom describes a situation in which we model a medical condition at a specific time interval, and the treatment decision is a one-time activity. A generic structure of this idiom is shown in Figure 5.8a. As we can see the condition, which depending on the clinical context can be the target, a comorbid condition etc, triggers the application of a treatment to prevent an adverse outcome.

2. *Treatment follow-up idiom*: this idiom describes a situation in which we model a dynamic treatment decision. Modelling multiple treatments means that we need to capture the disease progression and the effect of previous treatment strategies. A generic structure of this idiom is shown in Figure 5.8b. Similarly, with the treatment idiom, the trigger of the initial treatment is the initial state of the condition. However now the treatment affects the outcome indirectly through the state of the condition after the treatment. In addition, the response to the initial treatment becomes the trigger of the follow-up treatment. When capturing the disease progression over time given a series of treatments, modelling the before and after state of a condition is important.

Idioms can be used to connect the elicited variables. However, developing a large progressive BN in one go remains hard. As with all complex models, one solution is to divide the problem into sub-models and later combine them together (more details in section 2.3.1). During the expert knowledge elicitation, we proposed to divide the problem into smaller more tractable tasks. The same divisions can be used when modelling a progressive BN incrementally.

In this case study, the knowledge elicitation process was divided into the stages of care and the 5 main triggers: limb, pelvic, chest, abdominal and head injury. Thus, instead of building the full model at once, we developed sub models for each trigger separately. At first, we created the sub BN models for each trigger in stage 1 and then in stage 2. Taking the limb injury as an example, in Figure 5.9 we present the limb injury BN 1. With yellow we represent the evidence variables. The limb injury BN 1:2 is an extension of the BN 1

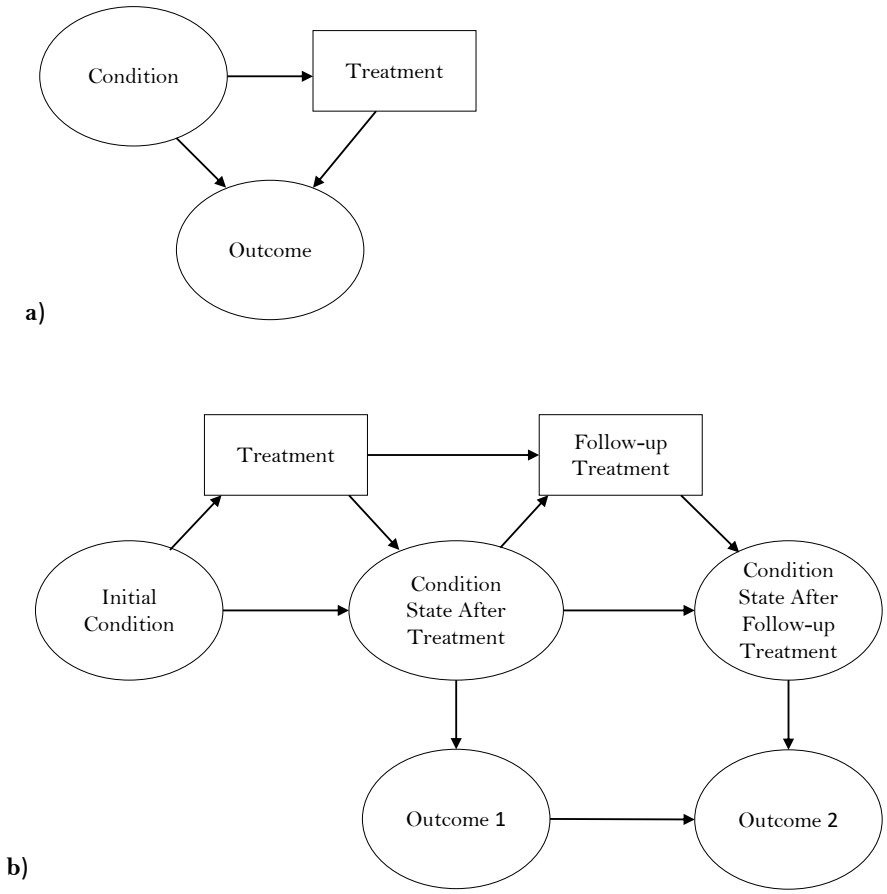

Figure 5.8: Different ways of modelling a treatment: (a) Treatment idiom, and (b) Treatment follow-up idiom

and it is presented in Figure 5.10. In purple, we represent the additional evidence variables that are available in stage 2. The treatment variables are presented with rectangulars. All the variables included in these two figures can be found in Table 5.2. The sub models for the remaining four triggers are shown in Appendix D.

Clinicians find easier to review smaller BN fragments than a large complex BN. When each sub-model is reviewed then we need to combine them all together. An way to 'piece' them together is to use variables that are common in all the sub-models. Variables that have the same name, definition and states can be considered as common. However, for combining the sub-models correctly we need to make sure that a common vocabulary among the elicited variables will be maintained. In Figure 5.11, we illustrate the combined limb and pelvic BN. The common variables that allowed us to connect the two BNs were the target death, as well as the mechanism of injury (MOI) and the physiological effects RR, SBP, HR, RR, and O2 Saturation. The combined BN is in APPENDIX E. The proposed progressive BN construction has been done 'by-hand' using AgenaRisk software. Software

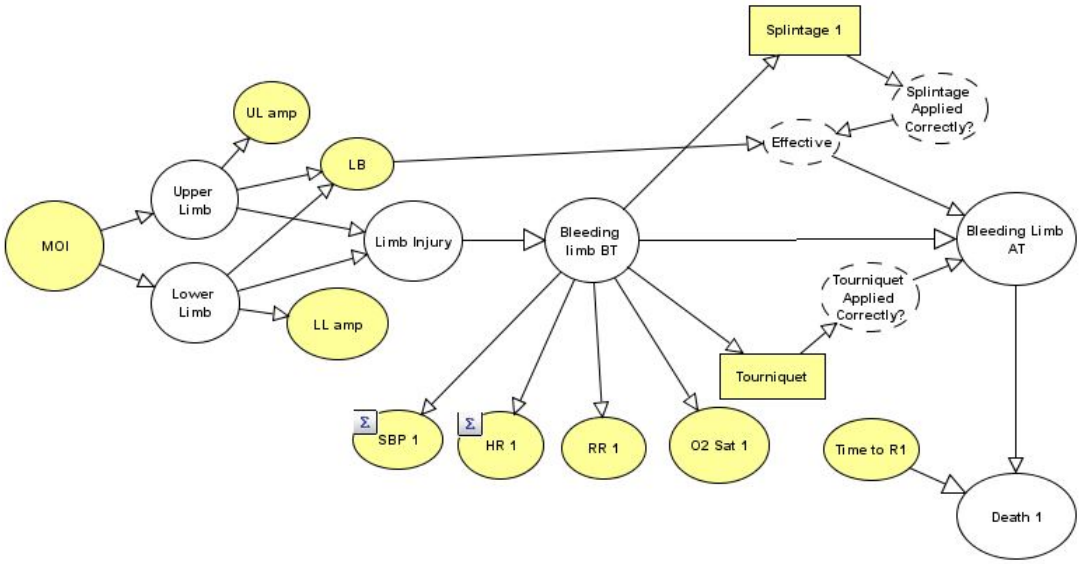

Figure 5.9: Limb injury BN 1

that allow a staged construction, such as GeNIe, can also be used.

5.5 Parameters: Learning and Elicitation

When the BN structure is reviewed and agreed, then the next step is to learn the parameters of the model. When few data are missing and they are missing at random (MAR), then the Expected Maximisation (EM) algorithm can be used to estimate them [149], [227], [56]. However, the parameter learning becomes more complicated when many data are missing, a situation very common in acute conditions. When many data are missing, then the estimation approaches become less accurate. For a discrete variable with more than 5% of their data missing, we can use a mixture of data and expert knowledge to learn its parameters:

$$\tilde{\theta} = r \times \theta_{knowledge} + (1 - r) \times \theta_{data} \tag{5.1}$$

Where $\theta_{knowledge}$ represents the parameters elicited from experts, θ_{data} represents the parameters learned from data, using EM algorithm for missing data, and r is a probability that represents the relative weight we give to the data versus the expert knowledge, such as $r = \frac{numberofmissingvalues}{totalnumberofcases}$. Imagine for instance that 12% of a variable's data are missing. Thus, we give 88% weight to the data and 12% weight to expert knowledge. This process is available in AgenaRisk software. For the variables that are not part of the dataset, then either we use mathematical formulas or logic functions, such as OR, AND, or nosy OR gates

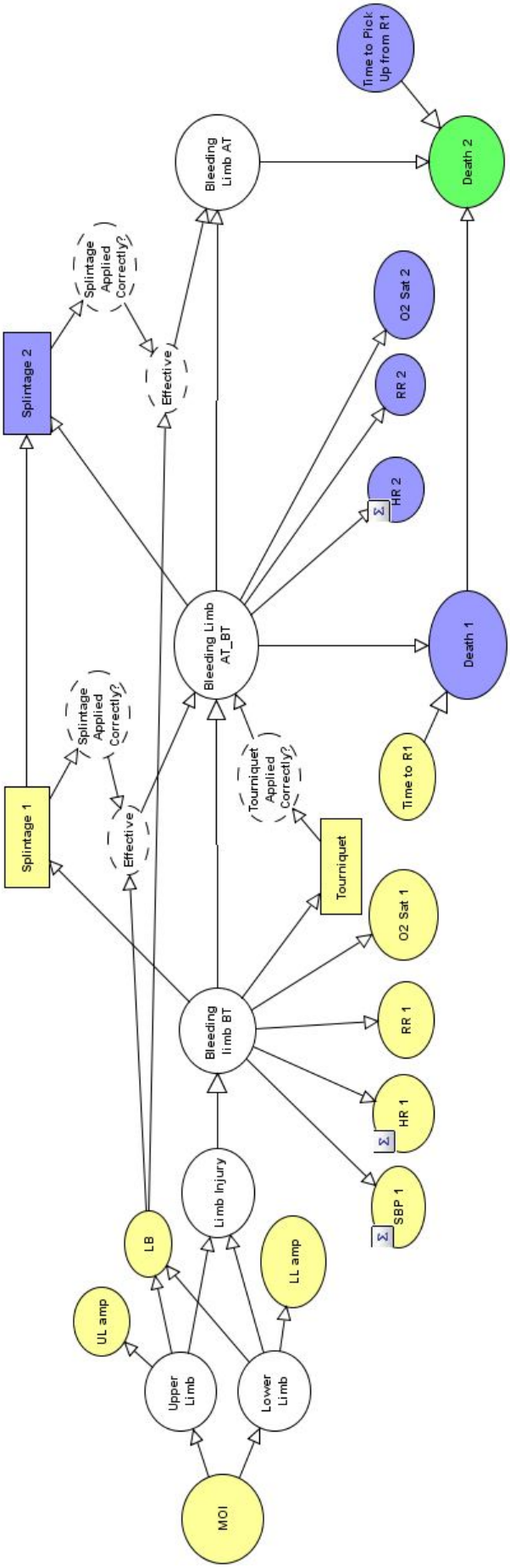

Figure 5.10: Limb injury BN 1:2

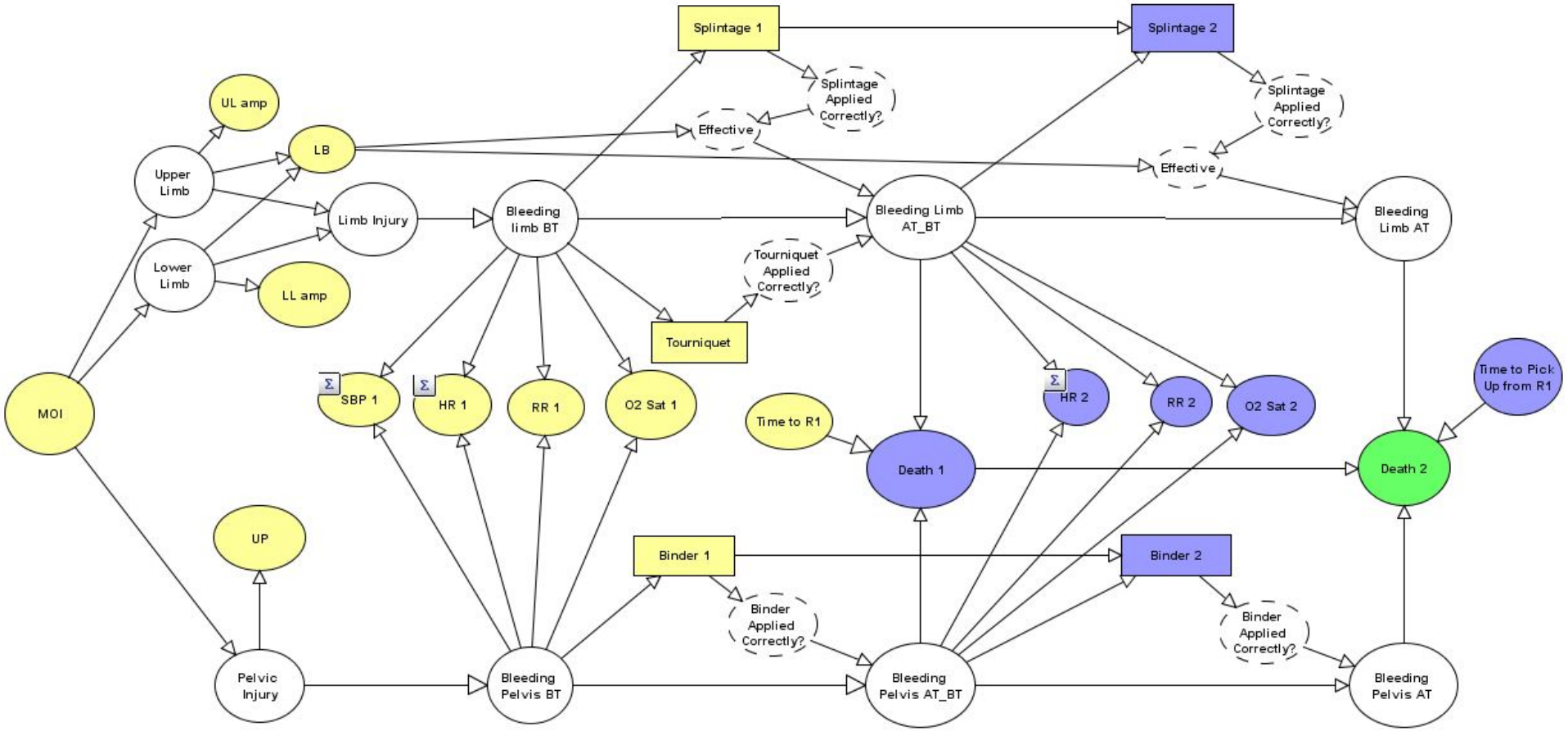

Figure 5.11: Combined limb and pelvic BN in stage 1:2

(see section 2.3.1) or we rely only on experts $(r = 1)$. The process of eliciting parameters from experts is divided into five stages: (1) select and motivate the experts, (2) structure the questions, (3) train the experts, (4) elicit experts' judgement and (5) verify the results (see section 2.3.1).

In this case study two experts were selected; SM that was involved in the development of the model's structure, and MM that had a good understanding of the model's structure and has a lot of experience as a military doctor (see Section 4.2.1). The next step was to structure the questions. Having different formats can be reassuring. Thus, three ways to describe the question and two formats for the answers were used. The question was described first using a BN fragment (Figure 5.12). As both of our experts were familiar with BNs and the model's structure, a BN fragment was enough to help them understand the conditional scenarios. In case, clinicians are not familiar with BNs an extra training process is required. This context was then translated into a simple conditional probability and a text using a likelihood format. Using the approach proposed by Van der Gaag et al., the answers were presented with a scale that had both numerical and vertical anchors (Figure 5.13) [82], [81]. Figures about the same conditional probability were grouped together to reduce the number of times a mental switch of conditioning context was required of the experts during the elicitation. The last step before the elicitation was to train the experts. At first, we informed the experts about the purpose of the elicitation and how we were going to proceed. Then the biases that they may face during the elicitation, such as base-rate bias or availability bias, were explained to them. Finally, we asked them to elicit two or three variables for which the frequency was known to see how close their answer was to the observed frequency.

The actual elicitation was performed with each expert separately and lasted an hour. During the elicitation, the experts had to judge not only one event but its complement as well. This step helped us to verify whether the elicited probabilities follow the law of probabilities. Having more than one expert giving their assessment independently means that more answers for each probability were available. Assessments by more than one expert can be handled in two ways: collect the assessment of each expert and combine the assessments into one, or have the experts come to an agreement. In our case study, we used the second option. In particular, a week after the initial elicitation we met both experts at the same time, we presented both of their answers and we asked them to come to a final agreement.

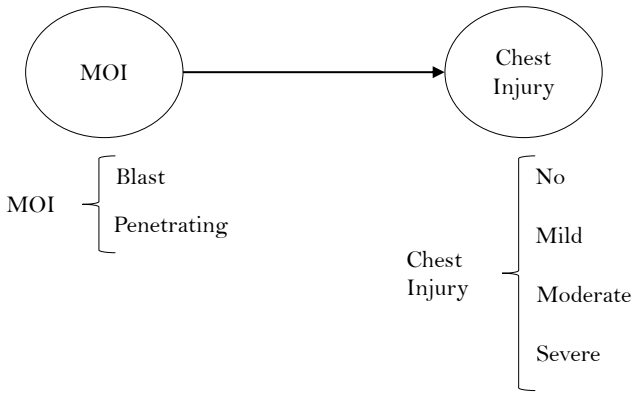

Figure 5.12: BN fragment that represents the conditional dependence between chest injury and the mechanism of injury (MOI)

When their initial answers were very different (only once), or they had a difficulty to come to a consensus (only twice), a third more experienced clinician, NT (see Section 4.2.1), was asked as well. During this stage, the three experts were together, the third more experienced clinicians reviewed the two answers, heard their justifications and then took the final decision.

When we have a progressive BN that models an evolving acute condition in successive stages of care we might have a different data size in each stage. Since not all the patients follow the same clinical pathways, sometimes only a subset of the patients treated in stage 1 is going through the stage 2. In such cases, the process of parameter learning should be done progressively. In this case study two databases were used; the joint theatre trauma registry (JTTR) database provided data in stage 1 and the medical emergency response team (MERT) database provided data in stage 2. In stage 1, 1227 cases were available in the JTTR database. More details on the exclusion criteria are available in Figure 5.14. From those cases, only 388 were picked up by the emergency care (stage 2). Those cases were part of the MERT database. To account for the two different data sizes, the parameter learning was done progressively. At first instance, 1227 cases were used to learn the parameters of the BN 1. Then, the parameters of the additional BN structure in BN 1:2 that captures stage 2 were learned using the 388 cases. Even if only a subset of the data was used to learn part of the parameters, experts believed that those picked up by the emergency care were a representative sample.

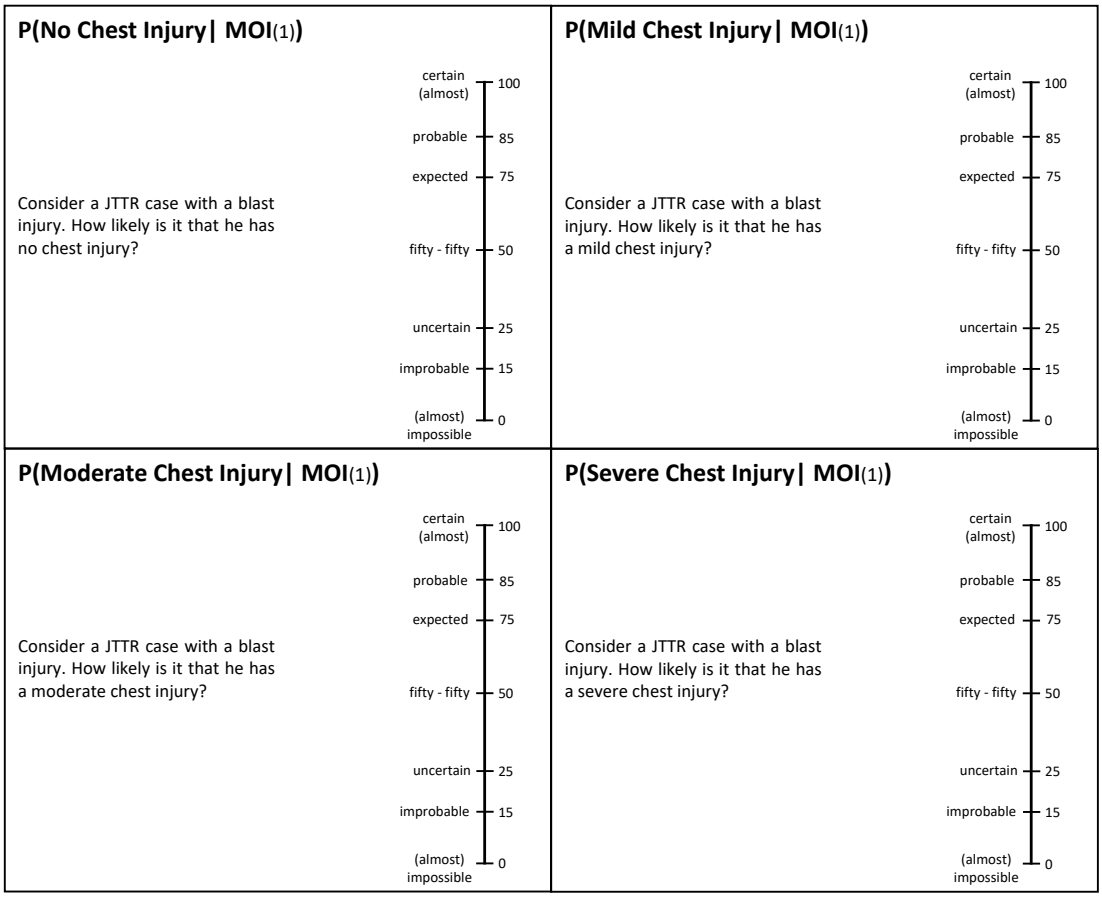

Figure 5.13: Format of questions and answers used during the parameter elicitation from experts

5.5.1 Learning the Treatment Effect from Observational Data

A particular case of parameter learning is when we learn the parameters of a treatment variable from observational data, when our aim is to capture its causal effect on the acute condition [102]. So far, we have described that the structure of the model was elicited from experts to ensure a causal coherence and a more complete representation of the actual world. In addition, we said that the model parameters were learned from observational data and/ or experts. It is not unusual to rely on observational data to perform observational reasoning. Questions such as 'What is the likelihood of survival knowing that the soldier has a lower limb amputation and an abnormal respiratory rate?' can be answered when we perform observational reasoning in a BN that has been trained from observational data (see Section 2.5.1).

The difficulty of using observational data arises when we want to learn causal relationships, such as treatment effects [124]. Normally, cause-effect relationships are learned from ex-

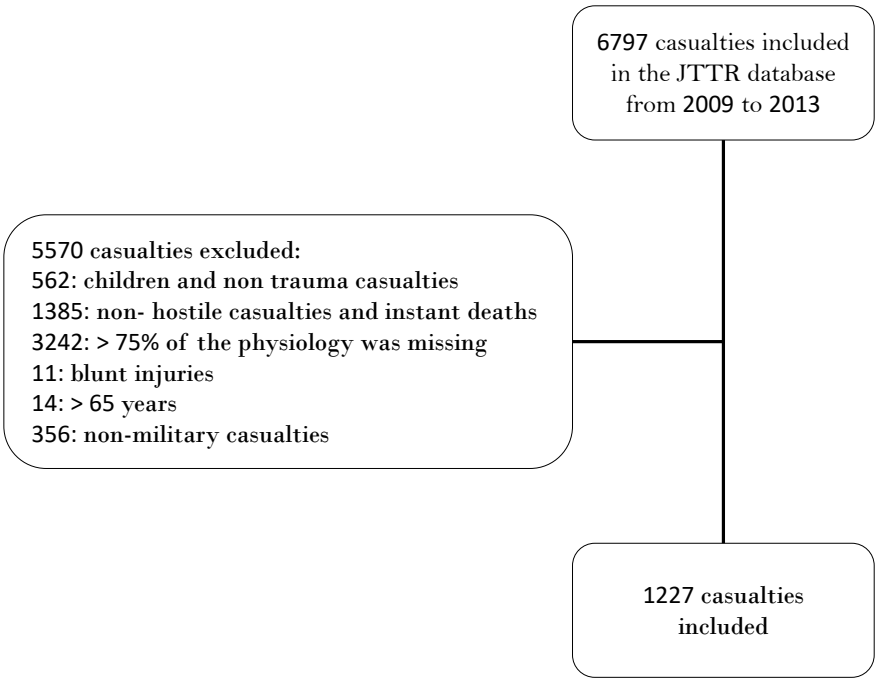

Figure 5.14: Exclusion criteria for the training JTTR database

perimental data derived from randomised control experiments [78]. The randomisation can be viewed as a way of sampling data by avoiding selection bias and confounding. A hesitation to endow observational associations with a causal interpretation is the lack of randomised treatment assignments. In observational studies, those receiving a treatment may be in a more severe condition than the untreated. Thus, an association derived from observational data would be a compromise between the truly beneficial effect of the treatment and the underlying greater risk in those who received the treatment. This is also known as confounding, which is the bias that arises when the treatment and the outcome share a common cause, and it is usually considered as the main limitation of observational data.

Imagine that we have a BN as shown in Figure 5.15. This BN follows the structure shown in Figure 5.8a, where L represents the severity of bleeding in the limb, T is the tourniquet and D represents death. We use this graph for simplicity, but the procedure that follows can be applied also to the more complicated structure shown in Figure 5.8b. The structure of the BN in Figure 5.15 is causal and the parameters have been learned from the 1227 cases in the JTTR database. The question that arises here is whether we can represent the effect of the observed treatment T on D when the parameters are learned from observational data.

In Figure 5.16, we can see that applying a tourniquet increases the soldier's chances of dy-

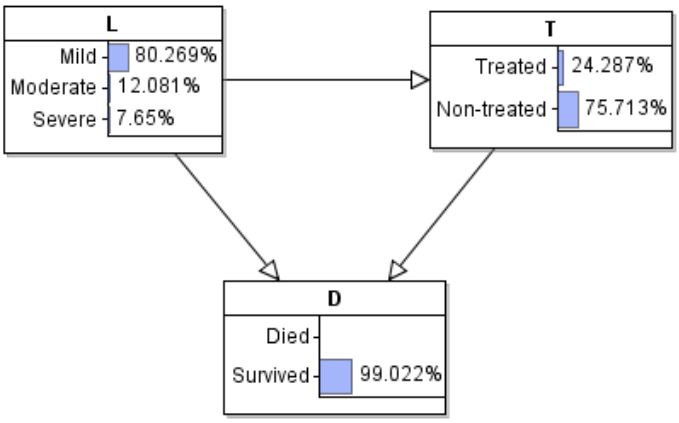

Figure 5.15: A BN fragment that models the effect of treatment T on the outcome D, sharing the common cause L

ing. In other words, variable L confounds the effect of treatment T on D. For having an unconfounding effect of T on D, we must suppress the effects of any exogenous variables (confounders) that influence both T and D. The variables T and D are unconfounded if and only if the following holds: $P(D = d|do(t)) = P(d|t)$ for all values $T = t$ and $D = d$. This equality states that T and D are not confounded when the association observed in the data between these two variables is the same as the association that would have been measured in a randomised control experiment, where T is randomly assigned [240].

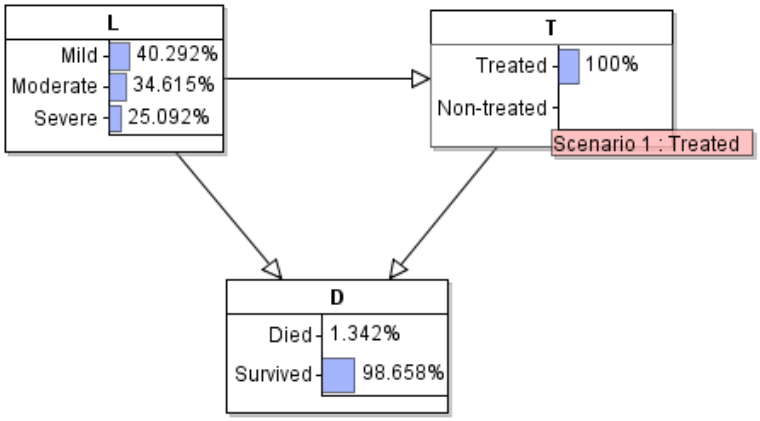

Figure 5.16: An example of how L confounds the effect of T on D

Looking at Figure 5.15, we can easily conclude that the equality is not correct since there is an open backdoor path between T and D ($T \leftarrow L \rightarrow D$). Clearly, we desire the unbiased estimate $P(D = d|do(t))$, but if only observational data are available, an unbiased estimate can only be obtained by 'adjusting' for all the confounding factors. One way to adjust for a confounder and have identifiable causal effects is to block the backdoor paths. In this ex-

ample, the backdoor path is blocked when the confounder L is observed. In such a case we have the following equality: $P(D = d|do(t)) = \sum_l P(d|t,l)P(l)$, which gives an unbiased estimate for the causal effect of T on D [240].

In our case study, L was not observed, so the backdoor path between T and D remained opened. However, we were still interested in the unconfounded effect of T on D. For that reason, we treated the observed treatment T as an intervention, [208]. In other words, we mimicked a randomised experiment where T was randomly assigned regardless L (see Section 2.5.2). The observation was transformed into an intervention that was independent to any other factor. As shown in Figure 5.17, the effect of tourniquet on survival is now beneficial.

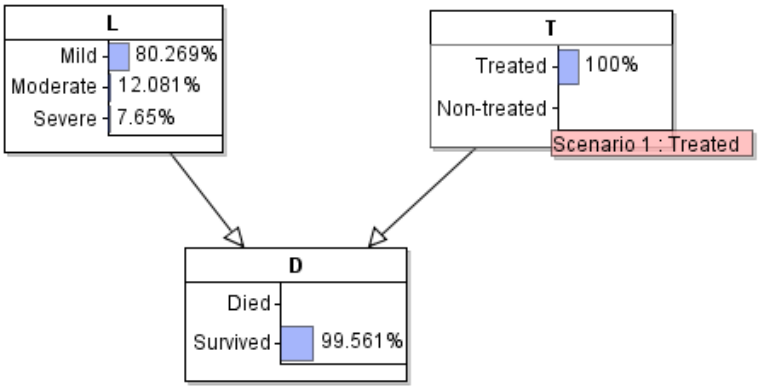

Figure 5.17: Interventional reasoning of T on D

To sum up, when the parameters of a BN have been learned from observational data and we want to estimate the effect of an observed treatment on the outcome, then a simple observational reasoning may be misleading. Adjusting for confounders is essential for having unconfounded estimates. As observational data are not controlled for confounders, alternative ways must be used. When the confounders are observed, their confounding effect is neutralised. However, when the confounders are unobserved, a solution is to use interventional reasoning that acts similarly with a randomised experiment. It is important to note that without a BN with a causally coherent structure, interventional reasoning is not possible (see Section 2.5.2).

5.6 Validation of the Model

The model's behaviour and performance were evaluated using two different ways: (1) a qualitative way, where we tested the model's behaviour in two extreme scenarios, and (2) a quantitative way, where we tested the average performance of the model.

5.6.1 Scenario-based Performance

First, a scenario-based validation was performed to understand how the model behaves, as well as the range of its predictions. The best and the worst-case scenarios were used as case studies. For generating the predictions in stage 1, the variables that were available within 5 minutes of the patient's arrival in the field care were instantiated. These variables are highlighted in yellow in APPENDIX E. In stage 2, the evidence in the field care and the additional information that was available within 5 minutes of the patient's arrival in the emergency care were instantiated. The additional variables are highlighted in purple in APPENDIX E. During the validation of the model, we still wanted to capture the causal effect of the observed treatments on survival. Thus, they were treated as interventions (see Section 5.5.1).

In the best case scenario the soldier was alive in both stages of care, and the evidence in stages 1 and 2 were:

- **Evidence Stage 1:** {MOI: Pent, Pen CW: No, HT: No, PT: No, Pen AW: No, UP amp: No, LB: No, LL amp: 0, UP: No, SF: No, GCS: 15, Chest Decompression: No, Tourniquet: No, Splintage: No, Binder: No, Time to R1: $<$ 1 hour, RR: Normal, O2 Sat: Normal, HR: 88, SBP: 127}
- **Evidence Stage 2**: {Evidence Stage 1, Death Stage 1: No, Chest Decompression: No, Splintage: No, Binder: No, GCS: 15, RR: Normal, O2 Sat: Normal, HR: 88, Pupil: Yes, Time to Pick Up: $<$ 10 min }

As we can see the soldier did not have any observed injury, his physiology was good and no treatment was applied, as it was not needed. Given the evidence, the probability of dying in stage 1 was *P(Death stage 1 = Yes| Evidence Stage 1) = 0.3%*. The prior probability of dying in stage 1, which represents an average situation, is *P(Death stage 1 = Yes) = 1.1%*. Therefore, in the observed scenario, the soldier has 0.27 times the risk of dying compared

to an average situation. In stage 2 the posterior of death is *P(Death stage 2 = Yes| Evidence Stage 2) = 1.45%*. Given that *P(Death stage 2 = Yes) = 1.55%*, we can conclude that in the observed scenario the soldier has 0.94 times the risk of dying compared to an average situation.

In the worst case scenario, we have two situations: (1) the soldier dies in stage 1, and the (2) the soldier dies in stage 2. The evidence variables in each stage are:

- **Evidence Stage 1:** {MOI: Blast, Pen CW: Yes, HT: Yes, PT: Yes, Pen AW: Yes, UP amp: Yes, LB: Yes, LL amp: 2, UP: Yes, SF: Yes, GCS: 3, Chest Decompression: No, Tourniquet: No, Splintage: No, Binder: No, Time to R1: $\geq$ 1 hour, RR: Abnormal, O2 Sat: Abnormal, HR: 111, SBP: 110}
- **Evidence Stage 2**: {Chest Decompression: No, Splintage: No, Binder: No, GCS: 3, RR: Abnormal, O2 Sat: Abnormal, HR: 111, Pupil: No, Time to Pick Up: $\geq$ 10 min}

Suppose that we want to predict the soldier's likelihood of dying in stage 1, then *P(Death stage 1 = Yes| Evidence Stage 1) = 56%*. In this scenario the soldier has 51 times the risk of dying compared to an average situation. Following that prediction, we observe after a while that the soldier dies in stage 1. Instantiating that evidence we have *P(Death stage 2 = Yes| Evidence Stage 1, Death stage 1 = Yes) = 100%*. Regardless the evidence in stage 1, if we observe that the soldier is dead in stage 1, then being dead in stage 2 is certain. Imagine that even if the risk of dying in stage 1 is high, the soldier stays alive in stage 1, but he dies in stage 2. If we don't instantiate the variable Death in stage 1, then we have *P(Death stage 2 = Yes| Evidence Stage 1, Evidence Stage 2) = 68%*. As expected the probability of dying increased even more. However, as mentioned in section 5.2, Death in stage 1 becomes an evidence in stage 2. In that case we have *P(Death stage 2 = Yes| Evidence Stage 1, Death stage 1 = No, Evidence Stage 2) = 1.8%*. The soldier has 1.1 times the risk of dying compared to an average situation. The likelihood of dying in stage 2 is slightly increased compared to an average situation, but it is much lower than the risk of dying in stage 1, which is paradoxical.

This scenario-based validation was used to test how the model behaves in specific situations. From the above results we can conclude that the model behaves as expected in stage 1. In stage 2, the model correctly identifies the increased or decreased risk of death compared

to an average situation. However, the posterior of death deviates very little from the prior of death, which in severe cases results in an unexpected decrease of the risk of death in stage 2 compared to the risk in stage 1. Investigating this behaviour further, we examined whether the model in stage 2 is able to understand the severe soldier's threat in the worst case scenario. Having *P(Overall Treat stage 2 = Severe| Evidence Stage 1, Death stage 1 = No, Evidence Stage 2) = 99.9%*, we conclude that the model can correctly identify the soldier's threat indicating that the flow of information from stage 1 to stage 2 is as expected. Therefore, the small deviation of the posterior of death from the prior of death in stage 2 might be justified by the small amount of cases, with a low proportion of deaths, used to train the model in stage 2. How this small deviation affects the model's performance will be explored at the end of the following section.

5.6.2 Overall Performance

This part of the validation was about the overall performance of the model. We applied a 10-fold cross validation [126]. This method divides the training dataset into 10 equal sized groups. Of the 10 groups, a single group is used as the test set, while the remaining 9 groups are used as training sets. The learning and testing continue iteratively until the model is validated with all the groups and a unique prediction is generated for each case. The cross-validation was done progressively as different data sizes were available in each stage of care. At first, only the BN 1 was cross-validated. Then, the parameters of the BN 1 learned from the full dataset were kept fixed and the additional part of the BN 1:2 that captures stage 2 was cross-validated. The predictive performance of the BN was assessed through the model's accuracy, discrimination and calibration [253], [252].

The overall accuracy of the model indicates how close the predictions are to the actual outcome. A measurement that is widely used to test the accuracy of a model is the Brier score [32]. The Brier score is the mean square difference between the predicted probability and the outcome. It can be applied to binary and categorical variables and it takes values between 0 and 1, where 0 indicates a perfectly accurate model as opposed to 1 which represents the worst-case scenario. The BN 1 and BN 1:2 have a Brier Score of 0.012 and 0.017, respectively. The accuracy of the model in each stage of care was also calculated as the ratio of all the correct predictions divided by the overall number of data. The best accuracy is equal to 1 whereas the worst is 0. The accuracy of the BN 1 and BN 1:2 was

0.74 and 0.28, respectively. A better insight on the model's performance in stages 1 and 2 is illustrated in the confusion matrix 5.3 and 5.4, respectively. In stage 1, the negative outcomes with prediction over 0.011, and the positive outcomes with prediction less than 0.011 were considered as the possibly inaccurate predictions since 1.1% of the soldier died in stage 1 and thus 0.011 was our prior probability. Similarly, the cut-off in stage 2 was 0.0155.

		Actual	
		Died	**Survived**
Predicted	**Died (Prediction $\geq$ 1.1%)**	11	319
	Survived (Prediction $<$ 1.1%)	1	896

Table 5.3: Confusion matrix for the BN 1

		Actual	
		Died	**Survived**
Predicted	**Died (Prediction $\geq$ 1.55%)**	0	271
	Survived (Prediction $<$ 1.55%)	6	108

Table 5.4: Confusion matrix for the BN 1:2

Accurate predictions discriminate between the patients with the event and those without. The discrimination of our BN was evaluated with the receiver operating characteristic (ROC) curve [285]. A ROC curve is a ranked order statistic for predictions against the true outcome. It is created by plotting the sensitivity, which is the true positive rate, against the specificity, which can be calculated as (1 - false positive rate). The area under the ROC curve represents the discrimination. An area of 100% represents a perfect test, while an area of 50% represents a very bad test. The area under the ROC curve is 0.89 (95% confidence interval (CI): 0.83-0.95) and 0.86 (95% CI: 0.77-0.94) for the BN 1 and the BN 1:2, respectively. Both ROC curves are illustrated in Figure 5.18.

The calibration refers to the agreement between observed outcome and the predictions on average. In other words, if the model is well calibrated and it predicts a 20% chance of survival, then the observed frequency of survival should be approximately 20%. The calibration of a model can be assessed using Hosmer-Lemeshow test [109]. This test divides

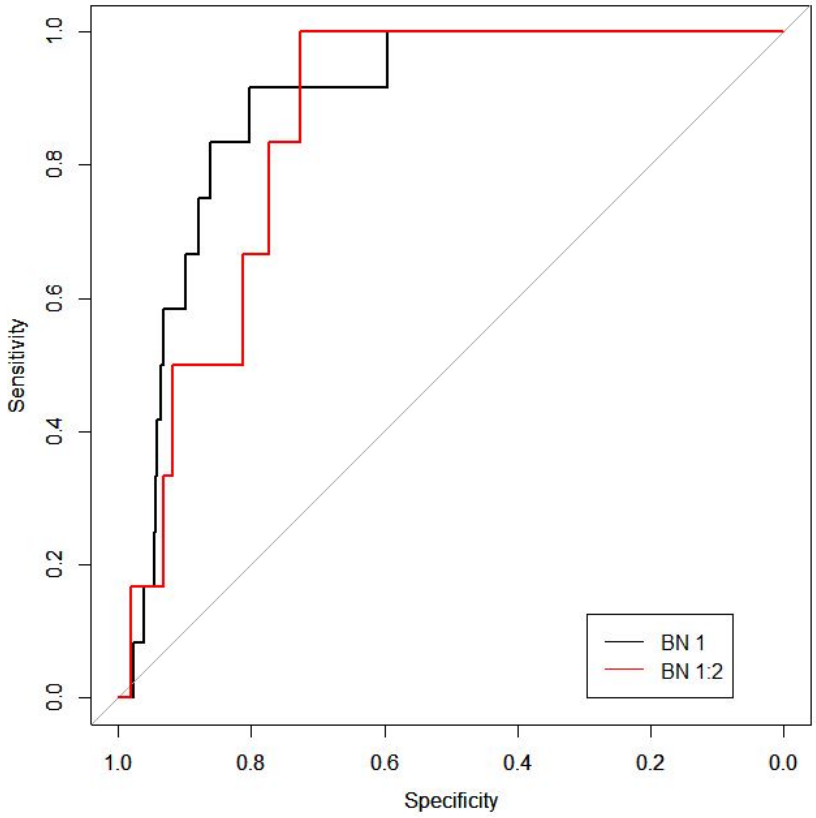

Figure 5.18: ROC curves for the BN 1 and BN 1:2

the data into 10 subgroups and calculates a chi-square statistic comparing the observed outcomes to the outcomes expected by the model in each subgroup. Low p-values indicate a lack of calibration. Hosmer–Lemeshow test is strongly influenced by the sample size. In large datasets, small differences between the expected and observed outcomes can lead to low p-values. The Hosmer-Lemeshow statistic of the BN 1 and BN 1:2 was 3.75 with a p-value = 0.88 and 28.8 with a p-value = 0.0004, respectively.

From all these tests we can conclude that the model's performance in stage 1 (BN 1) is good. However, the model in stage 2 (BN 1:2) does not perform well. Factors such as the much smaller amount of cases available in stage 2 with a low proportion of death, or the many missing values could potential justify this performance. Another factor that was highlighted during the scenario-based validation was the very small division of the posterior of death in stage 2 from the prior of death in stage 2. This might affect the number of true positives and true negatives in the cross-validated results.

As explained before, if a soldier died, a true positive is considered when the posterior exceeds the prior and vice versa. Regarding the cross-validated results, a true positive is

when the posterior in the cross-validated model exceeds the prior in the originally trained model. However, in many cases even if the posterior probabilities increased or decreased as expected, because of the small deviations, they were not higher or lower than the prior in the trained model to be characterised as true positives or true negatives. For instance, the prior of death in stage 2 in the trained BN was 1.55%. The prior in one of the cross validated models was 0.8% (only 3 deaths included in the training set). After instantiating the evidence for a fatality, the posterior in the cross-validated model was 1.4%. Even if the posterior was correctly increased, it was classified as false negative, because it was lower than 1.55%.

As our aim was to validate whether the developed BN can correctly identify the increased or decreased risk of the soldier's survival given the observed evidence and the initial life-saving treatments, we performed another 10-fold cross validation for the BN 1:2. However, this time, in all the cross-validated models we kept the prior probability distribution of death in stage 2 the same as the prior distribution in the originally trained model.

Using the same tests as before, we had an improved accuracy 0.72 compared to the previous accuracy 0.28. The confusion matrix 5.5 gives a better insight in the model's performance. In Figure 5.19, we can see the updated model's discrimination. The area under the ROC curve is 0.86 (95% CI: 0.75-0.96). Finally, as expected the model's calibration was improved. The Hosmer-Lemeshow statistic was 9.4 with a p-value = 0.31.

		Actual	
		Died	**Survived**
Predicted	**Died (Prediction $\geq$ 1.55%)**	5	108
	Survived (Prediction $<$ 1.55%)	1	271

Table 5.5: Confusion matrix for the BN 1:2, when the prior of death was kept the same in all the cross validated models

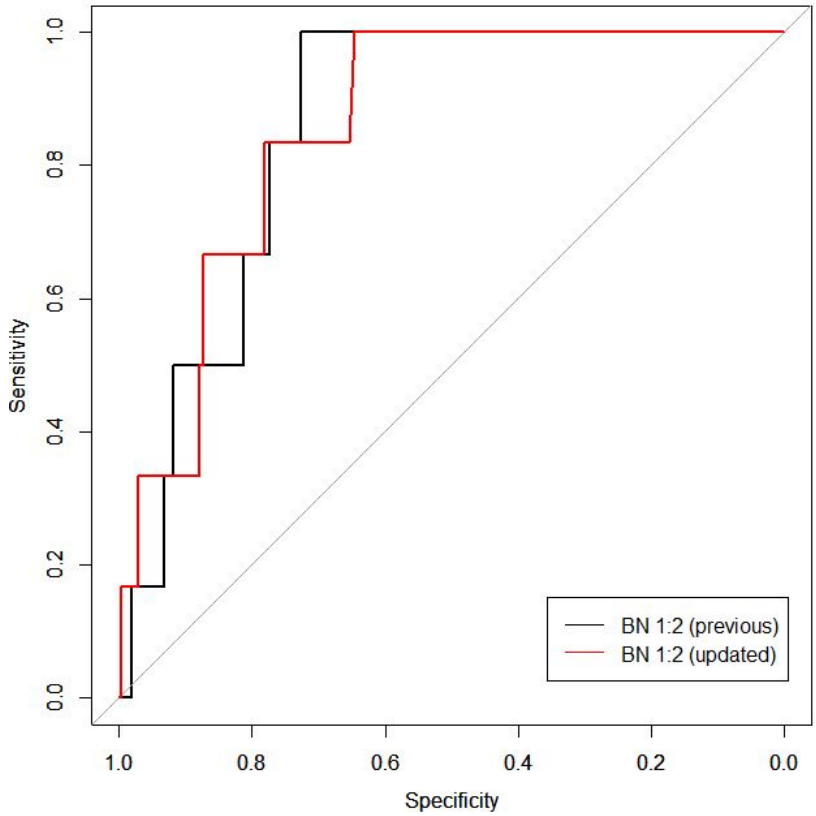

Figure 5.19: Comparison of the updated performance of the BN 1:2 with the previous one

5.7 Discussion

This chapter proposed a method for developing a progressive BN that models the rapidly evolvement of an acute condition, and captures the way clinicians gather information and make decisions in successive stages of care. The main characteristics of the proposed methods are: (1) the BN structure is non-stationary, (2) the structure and parameters of the model are not restricted to the available data, and (3) the time interval between two stages of care is irregular, following clinicians' timeline and not data availability.

While explaining the different components for developing a progressive BN, we addressed some important research challenges. At the beginning, we demonstrated a systematic way of eliciting and organising expert's knowledge. This knowledge allowed us to have a causally coherent and sufficient structure that it cannot always be obtained from observational data. In addition, we showed a way of incrementally translating the elicited knowledge into a BN. A great focus was given on how we model the unique treatment variables and learn their parameters from observational data, while assuring an unconfounded estimate. Finally, facing the problem of different data sizes, we explained how we can train

and validate a BN progressively.

All the above research challenges were demonstrated using the combat casualty model. The aim of the case study was to predict the mortality risk of a soldier given the observed symptoms, injury details and the effect of the initial lifesaving treatments in the highly uncertain prehospital setting. As British did not have their own Role 2 facility (see section 4.1.1), this was excluded from our model. Role 3 and 4 (see section 4.1.1) were out of the scope of this research as they represent a hospital care where there are multiple resources and the impact of the model is likely to be minimal. However, the proposed method can be extended to more than two stages of care.

The developed model helped us to demonstrate the steps that should be followed for modelling the progress of an acute medical condition. The model's performance in stage 1 (BN 1) was good. However, the performance of the BN 1:2 in the first cross-validation was not satisfactory. Having small deviations of the posterior probabilities of death in stage 2 from the prior probability of death in stage 2, we performed an additional cross validation, where we kept the prior probabilities of death in stage 2 the same in all the cross-validated models. This resulted in a significant improvement of the BN 1:2 performance. As a result, the BN 1:2 could quite accurately identify the increased or decreased risk of dying in stage 2, but with a very small deviation from the prior.

The model's performance could be improved by refining the model's structure [282] and/or correcting some of the many limitations of the data. One of the limitations is that our dataset may suffer from selection bias. Selection bias describes bias related to the way individuals are selected into the analysis. As we had many missing values for the physiological data (see Section 4.5.3), we selected only those cases with less than 75% of the physiological data missing (Figure 5.14). Even if the experts believed that the mechanism of those missing data was MAR, we can assume that a bias, potentially minor, was still present. For discrete variables with more than 5% of their values missing, we used a mixture of expert knowledge and data. However, this process was not followed for continuous variables with more than 5% of their data missing. EM algorithm was used instead. It is very likely that this is resulted in less accurate estimations [224], [235]. Either improving the data or advancing the elicitation process for continuous variables could significantly

improve the performance of the model. In addition, the amount of data used to train the part of the BN 1:2 that captures stage 2 was very small. Adding more data with a greater proportion of deaths might improve the problem of the small deviations. Finally, the original data described whether the soldier died or not without specifying when a death has occurred. Based on the available data and the original classification of the casualty, experts classified the casualty as survivor or fatality in each stage of the patient's care. However, this classification may not be always accurate. As a result, a more reliable capture of the time of death could result in a better performance.

Despite these limitations, we believe that the case study provided useful lessons to guide the future development of BNs that capture the progress of an acute condition and the dynamics of the clinical decision making. Future directions regarding the methodology are available in section 8.2.1. Regarding the case study, an interesting future step is to examine whether we can extend the developed BN in more than two stage of care to predict not only the likelihood of survival but also to provide treatment recommendations. In our case study we are in the prehospital environment, where we model some initial life-saving treatments. Having a treatment recommendation at this stage is not very useful. However, in the hospital setting, where more data are available, and more treatments are performed a treatment recommendation might be appropriate. In such a case, it would be appropriate to extend the BN to an influence diagram, where utilities are also modelled. Finally, studying how this model can be used in practice and potentially assist clinicians will be useful.

Chapter 6

Counterfactual Reasoning as a Healthcare Governance Tool

As explained in Chapter 4, the mortality and morbidity review meetings, conducted by the DMS, are considered as the bed-rock of quality improvement in combat trauma care. Currently, the review panel examines a casualty's salvageability and preventability using the clinical and military notes and the available trauma scoring systems. However, the existing trauma models cannot capture the progression of the soldier's condition given the clinical practice. In this chapter, using the BN developed in Chapter 5, we describe how counterfactual reasoning with BNs can be used as a healthcare governance tool to review treatment decisions and potentially assist the DMS mortality and morbidity review meetings.

6.1 Introduction

Counterfactual reasoning is likely to emerge when clinicians experience unexpected or undesirable outcomes [243]. In these circumstances, they may assess what would have happened if treatments other than the ones occurred had been selected. Imagine for example that a gynaecologist is deciding between prescribing drug A or drug B to a pregnant woman. She decides to prescribe drug A and the woman has a miscarriage after a week. Given that drug B was an option at the time, the gynaecologist mentally simulates what might have happened if she had selected drug B. Useful lessons can be learned by assessing decisions after they are made.

DMS mortality and morbidity review meetings are a fruitful ground for counterfactual rea-

soning. As explained in Section 4.6, the main aim of these meetings is to measure the performance of the UK deployed clinical services, such as assessment, treatment and evacuation of service personnel, and provide useful feedback. Based on the military and clinical notes and the available scoring systems, the review panel asks counterfactual questions to judge the quality of the clinical practice and investigates if anything better could have been done to prevent the undesirable outcome. However, the existing scoring systems can only be used as a description of the injury severity at a specific time point, either Role 3 or Role 4 (see Section 4.1.1 and 4.4). They cannot be calculated in the prehospital setting and they do not capture the consequences of the clinical practice. Moreover, clinicians' ability to perform counterfactual reasoning is not always optimal. Petrocelli et al. have explained that clinicians very often believe that a more desirable outcome could have or would have occurred if another decision had been selected [211]. However, this is not always true. In this chapter, we demonstrate how counterfactual reasoning with BNs can be used, alongside with the current practice, to assist clinicians' counterfactual reasoning and add extra assurance to the mortality and morbidity review meetings. In addition, we illustrate how counterfactual reasoning with BNs can be performed when we review treatment decisions in successive stages of the patient's care. To achieve our aims the BN developed in Chapter 5 is used.

This chapter is organised as follows: Section 6.2 gives the necessary background knowledge on counterfactual reasoning with BNs. In Section 6.3, we explain how we can perform counterfactual reasoning to review treatment decisions, where their effect migh belong to a later stage of care. Using three different queries, we illustrate in Section 6.4 how counterfactual reasoning with BNs can assist the DMS mortality and morbidity review meetings. Finally, a discussion is presented in Section 6.5.

6.2 Counterfactual Reasoning with Bayesian Networks

In counterfactual reasoning we want to explore the effect of a counterfactual event and compare it with the observed effect. The fact that the counterfactual event cannot be observed, so counterfactual reasoning cannot always be tested, has been one of the main criticisms on counterfactual reasoning [51]. Despite the objections, we believe that counterfactual reasoning is natural, and it is what makes human mind special [244]. These objections are addressed in more detail in the discussion.

Counterfactual events are based on causal relationships. Models that do not have a causally coherent structure cannot support counterfactual reasoning. As explained in Section 2.5.3, there are two main approaches for counterfactual reasoning with BNs: (1) the pruning theory proposed by Pearl [208], and the minimal-network theory proposed by Hiddlestone [103]. As we believe that the causal structure should not stay intact in the counterfactual world, only the pruning theory will be considered in this chapter.

According to pruning theory, the variable that we intervene upon in the counterfactual world should be independent of its causes. In other words, background inference from the intervened variable is not permitted. This gives rise to the question 'How can we store in the counterfactual world, the posterior probabilities that remain the same?'. Balke and Pearl proposed a graphical method, the use of a twin network, to answer this question [13]. In a twin network, one part represents the actual world, while the other represents the counterfactual world. As denotes the name, the two networks have identical structures, except for the arrows towards the variable that we intervene upon, which are missing in the counterfactual world. The variables that their posterior probabilities remain the same in both worlds are called background variables and they are shared between the two networks. The background variables help us to connect the twin networks.

Let us consider the BN presented in Figure 6.1. This is a fragment from the BN developed in Chapter 5 (see APPENDIX E for the full model). In this example, the target is the death in the field care. In the actual world, we observe that although the soldier had a severe limb injury, no tourniquet was applied, and the soldier died. Imagining a counterfactual world, we would like to know whether the soldier would have survived if we had applied a tourniquet. To answer the counterfactual question, we use a twin network as shown in Figure 6.2. In the counterfactual world (right hand side), the variable representing the Tourniquet intervention is disconnected from its parent following the graph surgery proposed by Pearl. The same arc is also removed in the actual world (left hand side) even though this is an observation. The reason follows from Section 5.5.1; if the back propagation is maintained then we infer from the non-application of a Tourniquet that the injury was not severe; this is not appropriate when evaluating the optimality of the intervention. We therefore reject the point of view that the treatment in the actual world should be simply treated as an ob-

servation, accepting that this would update our belief about the severity of the injury (in this case that the bleeding is mild since a tourniquet was not used), only for this belief to be further revise by the actual world outcome (here that the patient died). This point of view contradicts the aim of the counterfactual analysis which is to inform a review of potentially suboptimal treatment decisions. Altering the treatment decision cannot affect the variables that have not been caused by the intervention. As a result, all the variables that are an ancestor of the treatment, such as the actual injury, the state of bleeding BT and the related RR remain the same in the actual and the counterfactual world. These variables are used as the background variables. Depending on the available evidence, the model's structure and the counterfactual question, the background variables change.

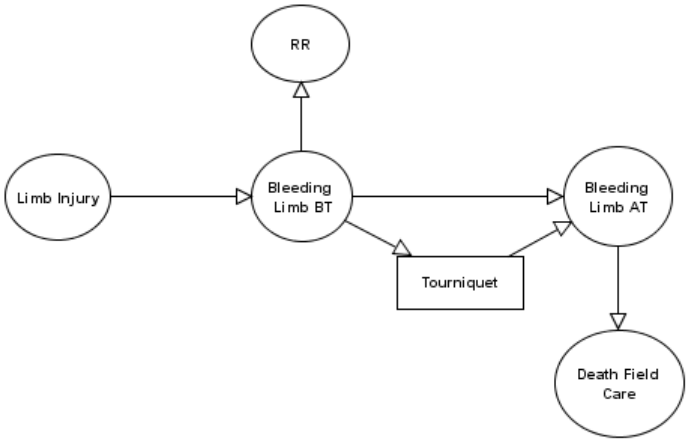

Figure 6.1: The initial BN model

6.3 Counterfactual Reasoning with Progressive Bayesian Networks

Many times, we might wonder if we had done something different at a specific stage what would have been the outcome at a later stage. In this section we extend the use of twin networks to perform counterfactual reasoning with BN for reviewing treatment decisions and their effects in successive stages of the patient's care.

To answer counterfactual questions related to treatment effects on variables that have been modelled as persistent (see section 5.3.2 and the treatment follow-up idiom in section 5.4), a causal BN that covers only one stage of care is not enough. A causal BN that models

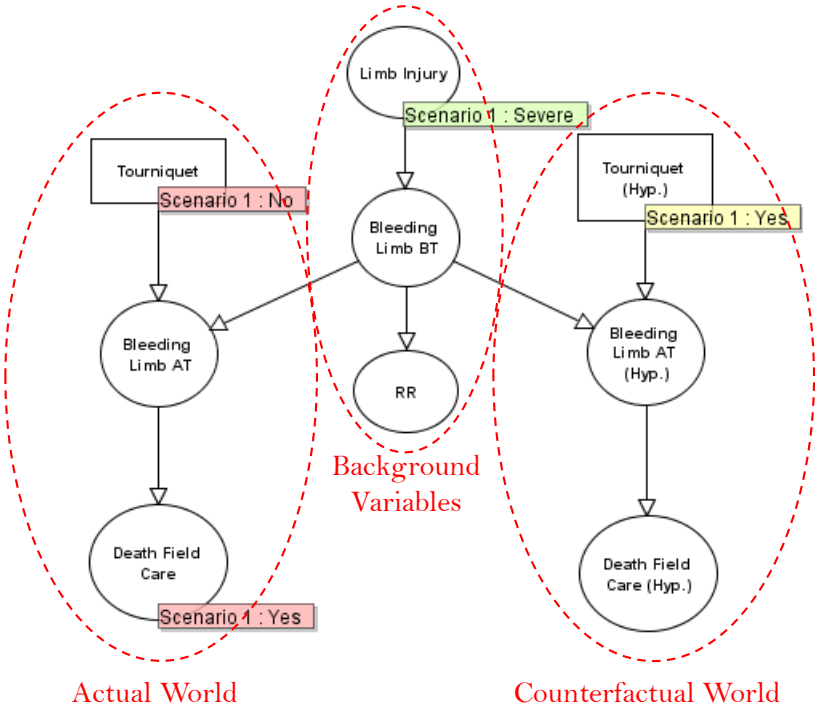

Figure 6.2: An illustration of the twin-network method on the BN shown in Figure 6.1

multiple stages of care is required. When we review treatment decisions in successive stages of care, the following counterfactual scenarios are possible:

1. Altered decision and its effect belong to different stages of care

2. Altered decision and its effect belong to the same stage of care

Suppose that we have the BN in Figure 6.3. This is again a fragment from the BN developed in Chapter 5. This BN captures the survival of an injured soldier in two successive stages of care: field care (t_1) and the emergency care (t_2). Let's consider the first scenario. In the actual word, we observe that the soldier had a severe limb injury, a normal RR and even if no tourniquet was applied in stage t_1, the soldier was alive at that stage. However, in stage t_2 his RR became abnormal and regardless the fact that a splintage was applied, the soldier died. A counterfactual question could be 'What is the likelihood that the soldier would have survived at stage t_2 if we had applied a tourniquet at stage t_1?'. We are wondering what would have been the outcome in stage t_2 if we had done something differently in a previous stage.

A twin-network can still be used to answer a counterfactual question where the altered decision and its effect belong to two different stages. The twin network that represents the

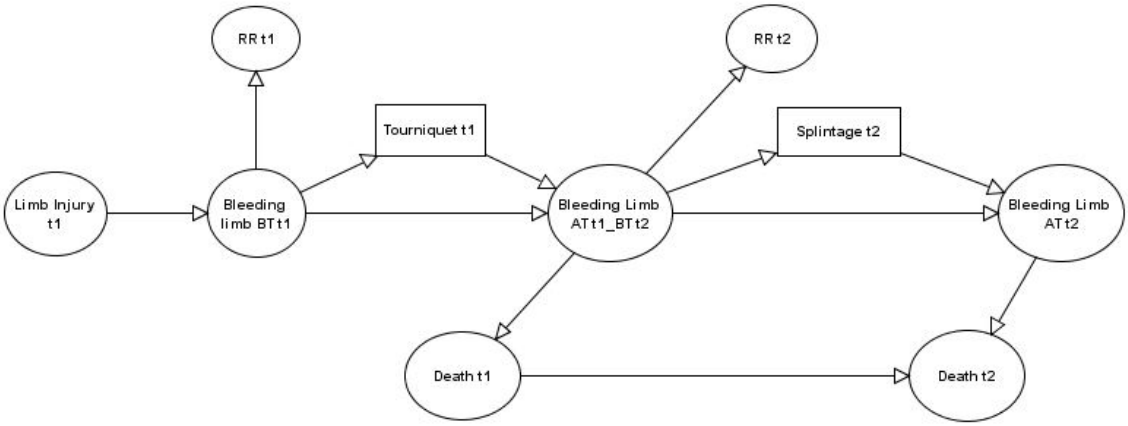

Figure 6.3: A BN fragment that captures the likelihood of survival in two successive stages of care

counterfactual question asked before is shown in Figure 6.4. Again, one part represents the actual world and the other part represents the counterfactual world. The variables that their posterior probability stays the same are the background variables. However, extra attention should be paid to all the evidence that follow the altered decision. Two important points that must be highlighted are:

1. In the counterfactual world all the variables that are influenced by the intervened variable, which in our case is tourniquet t_1, should be unobserved. For instance, we cannot assume that the RR will stay abnormal in t_2 if a tourniquet was applied at t_1. The same process of reasoning explains why the decision to apply a splintage at t_2 must be also unobserved.

2. The parents of the splintage at t_2 are not the same in the actual and the counterfactual world. In the actual world, the treatment variable is observed so its effect on the outcome is treated as an intervention to adjust for unobserved confounders (see Section 5.5.1). However, in the counterfactual world it is unobserved, so its structure should stay intact. Applying a splintage is influenced by the initial state of bleeding, so the arc that goes from bleeding to splintage should remain when the treatment variable is unobserved.

In the second scenario, where the altered decision and its effect belong to the same stage of care, then we can use two approaches. In case that nothing is observed at a later stage, then a twin network as described in Section 6.2 can be used. If, on the other hand, there is

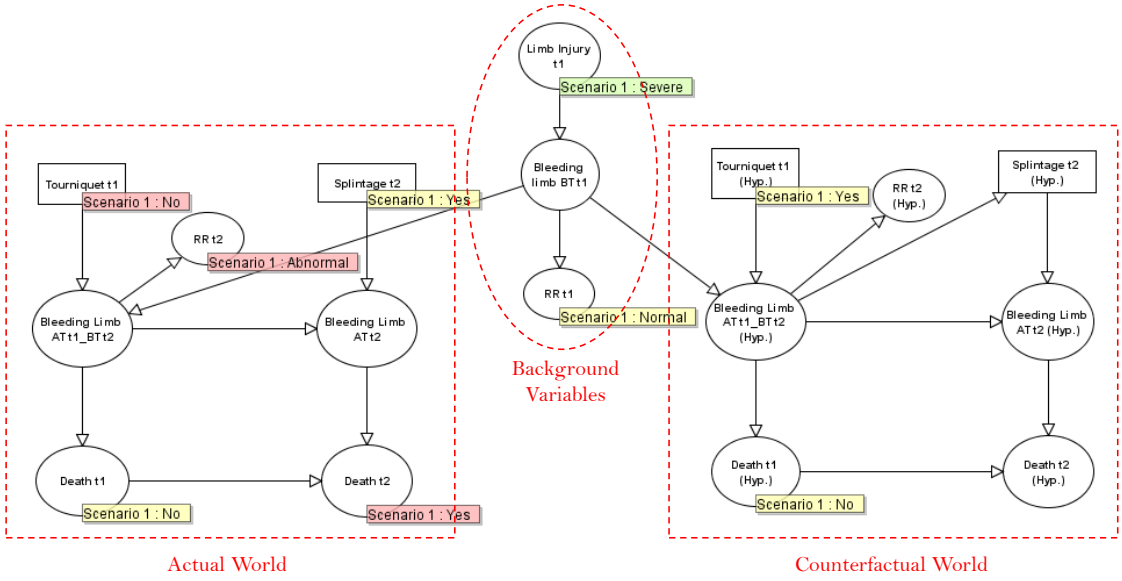

Figure 6.4: An illustration of the twin-network method on the BN shown in Figure 6.3

available information at a later stage, then the approach described in this section should be used instead.

6.4 Case Study

In this section we place counterfactual reasoning with BNs in the context of the DMS mortality and morbidity review meetings. During these meetings, a multidisciplinary panel reviews all combat casualties in terms of salvageability and preventability (see Section 4.6). Based on the clinical and military notes and the available scoring systems, the panel tries to imagine alternative scenarios and answer counterfactual questions. However, as explained in Section 4.4, the existing trauma models face several limitations. As a result, the aim of this case study it to provide an objective way to answer counterfactual questions related to the casualty's salvageability, which alongside with the available information and clinicians' judgement, can provide additional assurance to the current practice.

6.4.1 Scenarios

In this case study, we propose an alternative use of the BN developed in Chapter 5. We explain how we can use the same BN to review treatment decisions in successive stages of the soldier's care, and help clinicians to answer counterfactual questions. Following the scenarios described in Section 6.3, we illustrate our case study using three realistic

categories of query:

1. *Query A*: review an undesirable outcome in stage t_1 following a possibly suboptimal clinical practice in the same stage

2. *Query B*: review an undesirable outcome in stage t_1 following a reasonable clinical practice in the same stage

3. *Query C*: review an undesirable outcome in stage t_2 following a suboptimal clinical practice in the previous stage

The proposed categories of queries are not exhaustive, but are sufficient to explain how to answer different counterfactual questions asked during the DMS mortality and morbidity review meetings using twin networks.

Query A

The first query represents a situation where an undesirable outcome happens in the field care following a suboptimal clinical practice. Let's assume that there is an explosion in the battlefield and the soldier breaks his long bone and loses his right leg (below knee amputation). Despite the explosion, the soldier has no sign of a head injury; GCS = 14 and no skull fracture. There was no one near to help him so no tourniquet was applied, and the soldier died. Thus, we have the following set of evidence E: $\{$ *MOI = blast, UL amp.= No, LL amp.=1, LB = Yes, Tourniquet = No, GCS* t_1 *= 14, SF = No, Dead* t_1 *= Yes* $\}$. For simplicity all the other input variables are considered as unobserved. During the DMS mortality and morbidity review meeting the panel recognises that the soldier died from extensive bleeding and they wonder "If a tourniquet was applied, what would have been the likelihood of the soldier's survival?". Based on the clinical and medical notes, the review panel would probably have classified the casualty as potentially salvageable (S2) (see section 4.6). As this scenario takes place in the field, the BN in the first stage is sufficient to answer the counterfactual question (APPENDIX E). Using a twin network, we illustrate both worlds in Figure 6.5. In this query only limb and head injury are considered. This is why there are many background variables and most are unobserved. The variables that follow the changed decision, applying a tourniquet, are duplicated in both the actual and the counterfactual world. In the counterfactual world, the soldier would probably have survived if a tourniquet had been applied. Using the relative risk, we could say that the soldier in the counterfactual world has $\simeq 0.14$ times the risk of dying compared to a similar

situation when a tourniquet was not applied and $\simeq 2$ times the risk of dying compared to the prior, which represents an average situation. Both risks have been calculated as follows:

$$\frac{P(Deadt_1(Hyp.)=Yes|E,do(TourniquetHyp.)=Yes)}{P(Deadt_1(Hyp.)=Yes|E,do(TourniquetHyp.)=No)} \tag{6.1}$$

$$\frac{P(Deadt_1(Hyp.)=Yes|E,do(TourniquetHyp.)=Yes)}{P(Deadt_1=Yes)} \tag{6.2}$$

Not applying a tourniquet was catastrophic. Having the prediction produced by counterfactual reasoning can reassure clinicians that their classification was sensible. In addition, useful lessons can be learned to support better future decisions and clinical guidelines, such as not controlling haemorrhage as soon as possible could be fatal.

Query B

The second query is similar to the previous one but now the soldier is also unconscious (GCS = 3) and has a deep skull fracture. No tourniquet was applied, and the soldier died. Thus, the set of evidence is *E:* $\{$ *MOI = blast, UL amp.= No, LL amp.=1, LB = Yes, Tourniquet = No, GCS* t_1 *= 3, SF = Yes, Dead* t_1 *= Yes* $\}$. Here, the review panel wonders again about the effect that a tourniquet would have had on the survival of the soldier. The classification here is not straightforward. Except for bleeding, the soldier has also a severe head injury. The review panel classifies the casualty as possibly salvageable (S3). Using the same process as before, we alter the state of tourniquet and we observe the likelihood of dying. The twin-network presented in Figure 6.6 illustrates both worlds. In the counterfactual world, applying a tourniquet reduces the risk of dying because of bleeding, but the soldier is still likely to die because of the head injury. In particular, the soldier in the counterfactual world has $\simeq 0.22$ time the risk of dying compared to a similar situation when a tourniquet was not applied and $\simeq 13.3$ times the risk of dying compared to the prior. Thus, not applying the tourniquet may not have been decisive in these circumstances.

Query C

The third query is an extension of the first query. We have the same injury and symptoms in the first stage, a tourniquet was not applied in the first stage, but the soldier survived and was picked up by the helicopter (second stage). At that point his GCS was worse (GCS = 6) and even though they applied a splintage the soldier died in the helicopter. Thus, the set of available evidence is *E:* $\{$ *MOI = blast, UL amp.= No, LL amp.=1, LB = Yes,*

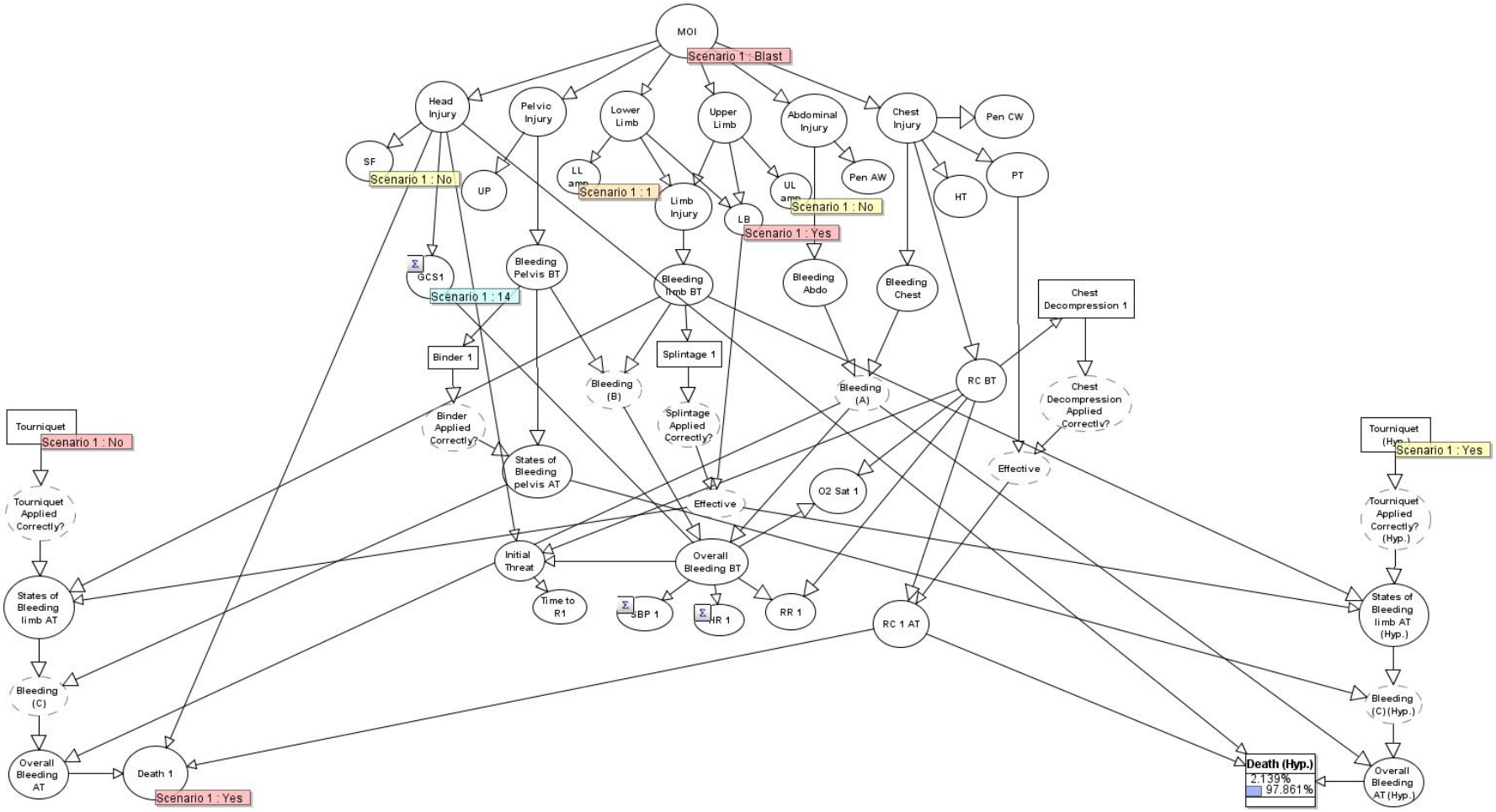

Figure 6.5: Twin-network for query A

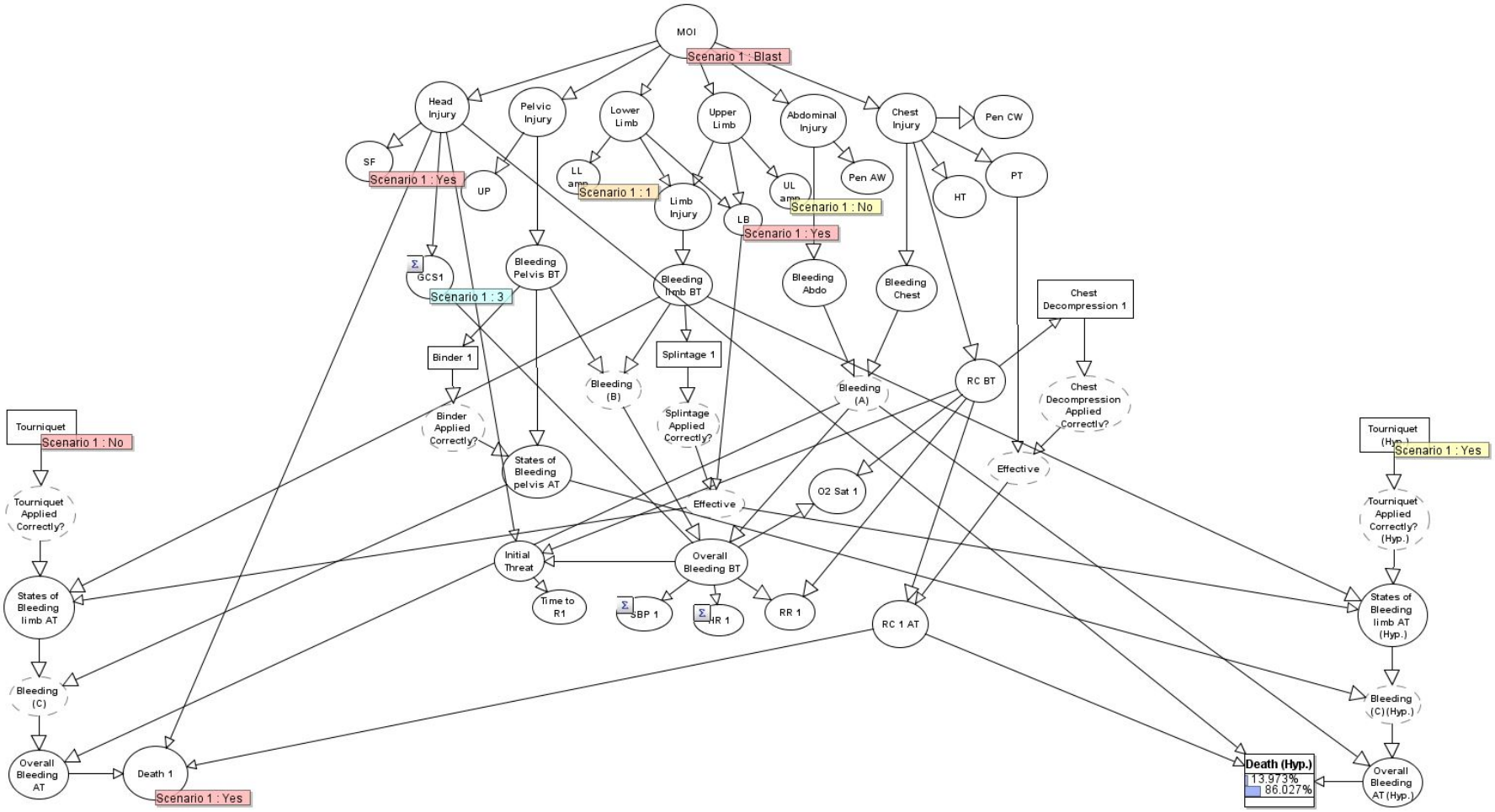

Figure 6.6: Twin-network for query B

Tourniquet = No, GCS t_1 = 14, SF = No, Dead t_1 = No, GCS t_2 = 6, Splintage t_2 = Yes, Dead t_2 = Yes}. Now the review panel wonders whether applying a tourniquet at the first stage, would have saved the soldier's life. The twin-network presented in Figure 6.7 illustrates both worlds. In this scenario the full BN is used (APPENDIX E). As explained in section 6.3 all the decisions and evidence that happen after the intervened variable are unobserved in the counterfactual world. However, since the comparison focuses on the effect of the alternative decision on the oucome in stage t_2, we must assume that in the counterfactual world the soldier survived in stage t_1. In the counterfactual world the soldier has $\simeq 0.97$ times the risk of dying compared to a similar situation when a tourniquet was not applied in the first stage and $\simeq 0.98$ times the risk of dying compared to the prior. Thus, in this alternative scenario, the soldier would have been more likely to have survived in the helicopter if a tourniquet had been applied in the previous stage.

6.5 Discussion

This chapter is an initial attempt to explain how counterfactual reasoning with BNs can be used as a healthcare governance tool to assess what would have happened if treatments other than those occurred had been selected. The novelty of this chapter can be summarised as:

1. We extended the use of counterfactual reasoning with BNs to review clinical decisions, where the alternative treatment strategy and its effect belong to different stages of the patient's care.

2. We placed counterfactual reasoning in a specific clinical context, such as the DMS mortality and morbidity review meetings to provide a more objective answer regarding casualty's salvageability.

Using the progressive BN developed in Chapter 5, we demonstrated how we can answer counterfactual questions about treatment effects on variables that have been modelled as persistent. The described logic, which says that all the evidence and decisions influenced by the variable that we intervene upon should be unobserved in the counterfactual world, can be extended to a BN that models more than two stages of care. In addition, we believe that the proposed approach is applicable to other time-based methods, such as DBNs. As the creation of twin networks is not yet automate, only three realistic queries have been

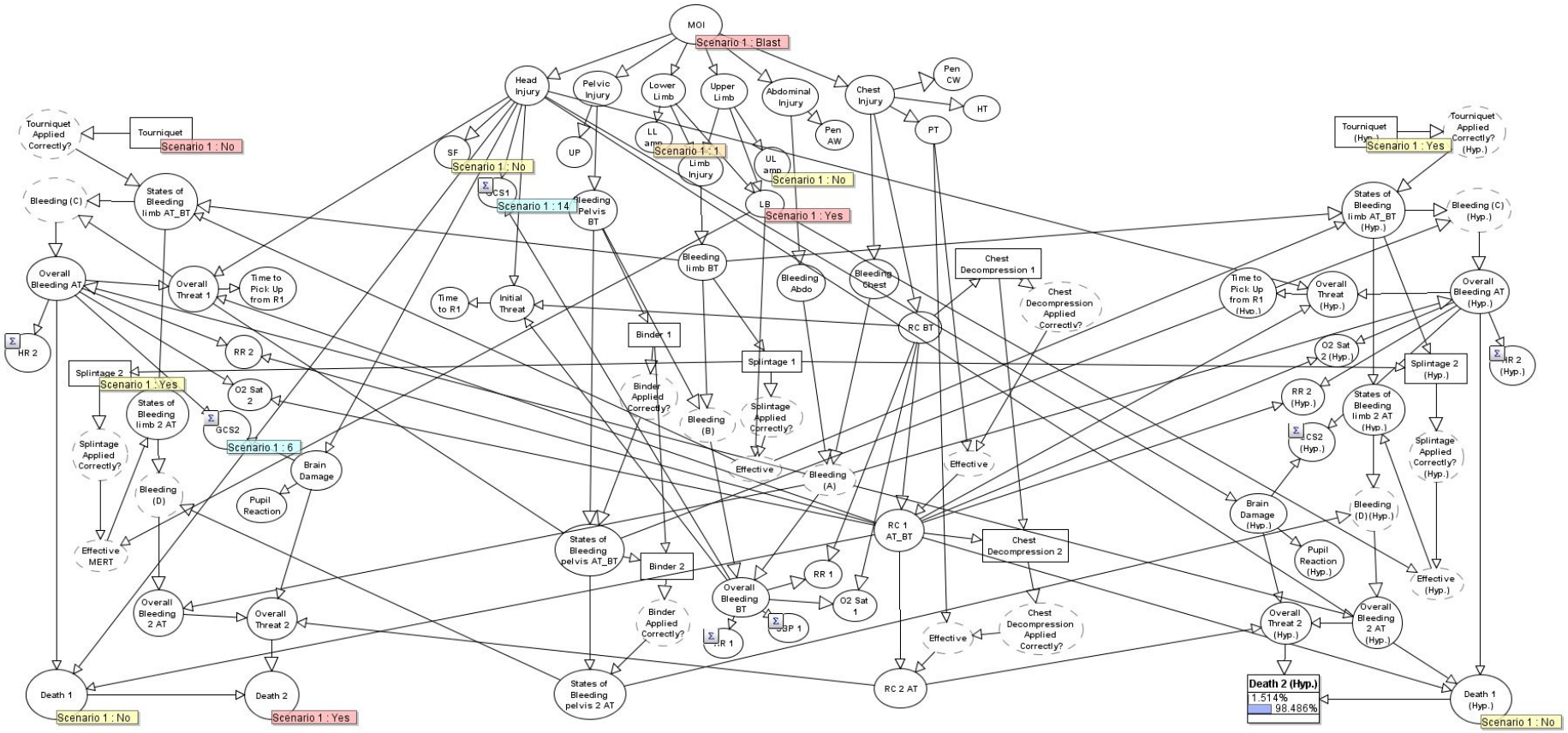

Figure 6.7: Twin-network for query C

used to illustrate how the proposed counterfactual reasoning with BNs could be used as an additional tool, alongside with the existing clinical and military notes, to assure an effective conduct of the DMS mortality and morbidity review meetings. However, when the creation of twin networks is fully automated, it could be useful to apply counterfactual reasoning to many real cases and potentially detect cases where treatment should have been different. Although, we used a military environment, this work can be easily extended to the civilian sector, as mortality and morbidity review meetings are conducted regularly there as well [104].

Despite the benefits of counterfactual reasoning there are some objections. Dawid in his paper 'Causal Inference Without Counterfactuals' started a long debate among scientists [51]. Apart from his paper, seven more commentaries as well as his one rejoinder can be found in the same publication. Dawid questioned the scientific validity of counterfactual reasoning and said that 'I have argued that any elements of a theory that have no observable or testable consequences are to be regarded as metaphysical and should not be permitted to have any inferential consequences either'. Both Cox and Pearl explained in their commentaries that any counterfactual assumption should not be pressed too far beyond the limits of which they can be tested. In addition, they both claimed that several aspects of counterfactual reasoning can be either directly tested or at least they are indirectly testable via their consequences. Pearl explained that 'If our conclusions have no practical consequences, then the sensitivity to invalid assumptions is totally harmless and Dawid's warning is harmless. If, on the other hand, our conclusions do have practical consequences, then the sensitivity to assumptions automatically makes those assumptions testable.' Dawid in his rejoinder, although he was still opposed to counterfactual reasoning, he agreed with Pearl's argument and accepted the fact that no problem exists when the counterfactual assumption have testable implications.

In this chapter, counterfactual reasoning followed the way clinicians review past decisions. Clinicians may try to remember old, similar cases that they came across during their careers, where alternative decisions were taken. The observed consequences of those past decisions are used as a verification of their counterfactual reasoning. In addition, we used counterfactual questions for unexpected or undesirable outcomes. Those outcomes should probably be the minority and more similar cases, where the clinical practice is optimal, and the outcome is desirable, can be used to test the counterfactual world. Except for poten-

tially testable counterfactual events, we focused only on realistic counterfactual questions. Similarly with Dawid, metaphysical or unrealistic counterfactual questions, such as 'If the soldier had a normal heart rate, would he still be dead?' were not considered, as it is impossible to alter directly the heart rate. Finally, we aim counterfactual reasoning to be used alongside with clinicians' judgement and not to replace them. Taking all these factors into consideration, we believe that if the counterfactual questions asked are realistic and ethical, then there is no harm in using counterfactual reasoning with BNs as a healthcare governance tool.

Chapter 7

An Incremental Explanation of Inference in 'Hybrid' Bayesian Networks for Increasing Model's Trustworthiness

An issue that is regularly neglected is the trustworthiness of the model. A model is less likely to be used if clinicians do not understand how it reasons. A BN has the advantage that is not a black-box and its reasoning can be explained. As described in Section 3.3, several approaches have been proposed to explain the reasoning of a BN. However, there are many situations where the existing methods cannot be applied. In this chapter, we propose an incremental explanation of inference that can be applied to hybrid BNs that contain both discrete and continuous nodes. The key questions that we answer are: (1) which important evidence supports or contradicts the prediction, and (2) through which intermediate variables does the information flow. The explanation is illustrated using a BN designed for predicting coagulopathy in the ED. A small evaluation study is also conducted.

7.1 Introduction

Sometimes it is assumed that an accurate prediction is enough for making a CDS model useful, but this neglects the importance of trust (see Section 3.3). A user, who does not understand or trust a model, will not accept its advice [276], [175]. Giving users an explanation of the model's reasoning may make its predictions easier to trust.

In contrast to many CDS models, a BN is not a black box and its reasoning can be explained. Many methods of explaining the reasoning of a BN have been proposed [138]. The common ground of these methods is the identification of the most important/ influential evidence and the chains of reasoning between the evidence and the target (see Section 3.3.2). Despite their benefits, the proposed techniques are not always applicable (see Section 3.3.3). In this chapter, we propose a practical method of explaining the reasoning in a BN, so that the user can understand how a prediction is generated. Our proposed method can be used in hybrid networks that have both continuous and discrete nodes and requires no user input. In addition, we simplify the process of identifying the most important evidence and chains of reasoning, so we can be able to produce rapidly a good and concise explanation, but not necessarily the most complete one. In fact, our method produces an incremental explanation that has three successive levels of detail. The key questions that we answer are: (1) which important evidence supports or contradicts the prediction, and (2) through which intermediate variables does the information flow. A clinical case study on predicting coagulopathy in the ED is being used to illustrate our explanation. An evaluation study of the impact that the explanation has on clinicians' trust is also presented using the same case study.

This chapter is organised as follows: in Section 7.2 we describe in detail the proposed method. The verbal output of the explanation is presented using a real scenario in Section 7.3. In Section 7.4, we describe a small evaluation study and its results. Finally, a discussion is presented in Section 7.5.

7.2 Generating an Incremental Explanation of Reasoning in Bayesian Networks

This section presents the proposed method for generating an incremental explanation of reasoning in BNs. At the beginning, an overview of the method is presented. Then, each level of the explanation is described in detail.

7.2.1 Overview

The aim of our method is to produce an explanation that can help the end user to understand the model's reasoning and be able to accept or reject its advice. At the beginning, we have a target variable (T) that we try to predict based on a set of observed evidence (E). The variables that are included in the explanation are called the explanatory variables X. The set of X consists of a set of significant evidence E_{sig}, which are d-connected to T and have a significant impact on it, and a set of intermediate variables (X_I) that are unobserved (i.e. not evidence variables) and act as a middle step in the flow of information from E_{sig} to T. The different sets of variables are shown in Figure 7.1.

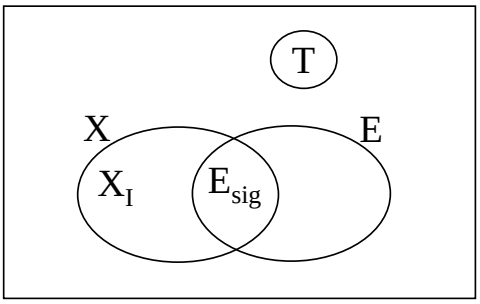

Figure 7.1: Variables in the explanation of reasoning

The explanation has three levels of increasing detail (Figure 7.2):

1. The first level lists the significant evidence variables E_{sig}, ordered by their impact on T. The variables presented in this level are grouped into two clusters based on whether they support or conflict with the effect of the combined evidence. More details are available in Section 7.2.2.

2. The second level identifies the intermediate variables X_I through which the information from E_{sig} to T flows and it shows how the evidence has changed the probability distribution of X_I. More details are available in Section 7.2.3.

3. The final level describes the effect that each E_{sig} has on each of the intermediate variables X_I, supporting or conflicting with the combined effect. More details are available in Section 7.2.4.

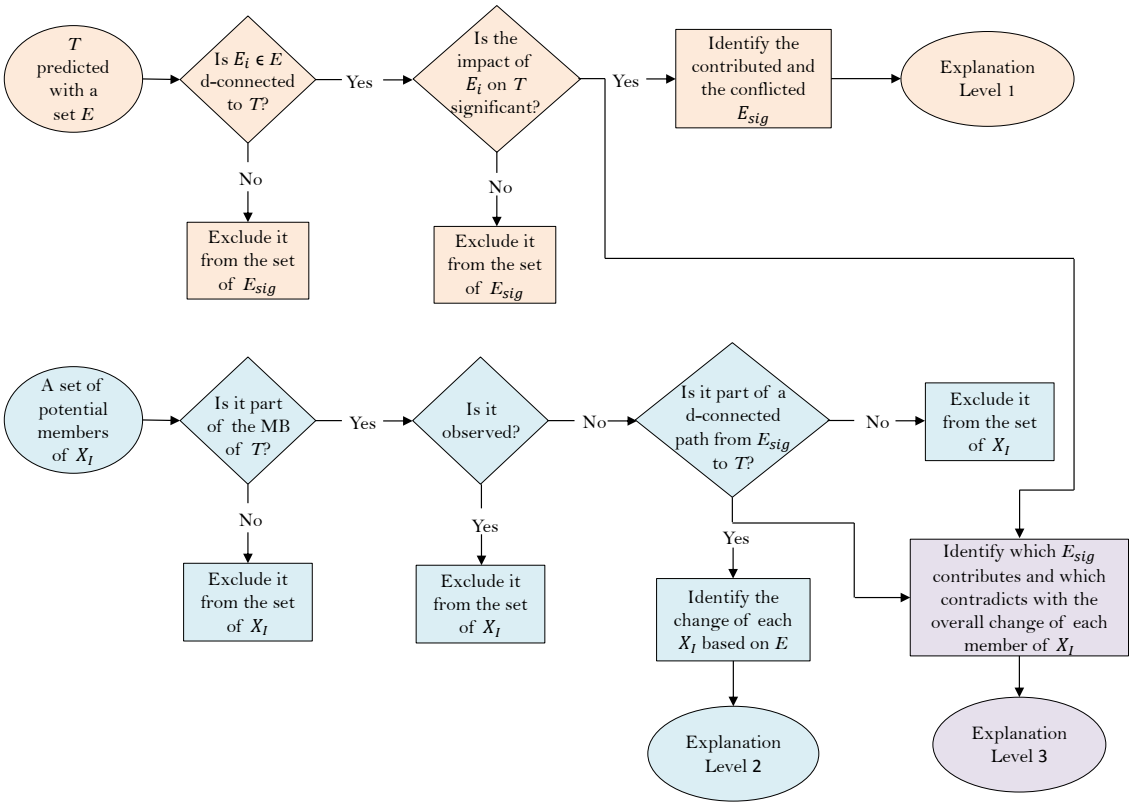

Figure 7.2: The process of the proposed explanation of reasoning

7.2.2 Level 1: Significant Evidence Variables

In the first level of the explanation, we try to answer the question 'How does each evidence affect the target?'. Answering that question requires first a measure of impact, then a threshold of significance and finally an analysis of whether each evidence supports or conflicts with the overall change.

Evidence Impact on the Target

Following INSITE [254], the impact of an evidence variable E_i relates to the distance between the posterior probability with all the evidence ($P(T|E)$) and the marginal posterior probability when E_i is excluded from the set of evidence ($P(T|E \backslash E_i)$), such as:

$$\mathrm{Im}_E(E_i) \triangleq D(P(T|E)||P(T|E \backslash E_i)) \tag{7.1}$$

INSITE uses the KL divergence as the distance metric. However, it is not always well defined. In our method, we measure the difference between the two distributions using the Hellinger distance (D_H). Given two discrete distributions $P = (p_1, \dots p_n)$ and $Q =$

$(q_1, \ldots, q_n)$, Hellinger distance is defined as:

$$D_H(P,Q) = \frac{1}{\sqrt{2}}\sqrt{\sum_{i=1}^{n}(\sqrt{p_i} - \sqrt{q_i})^2} \tag{7.2}$$

Hellinger distance is symmetric, non-negative and it satisfies the triangle inequality. Its range is between 0 and 1. This distance metric was used because:

1. *It can be calculated for both discrete and continuous distributions*: Having a distance metric that can be applied to both discrete and continuous distributions is fundamental, as nowadays most networks are 'hybrid'.

2. *It is u-shaped*: A u-shape metric gives a greater penalty to the distance from 0.9 to 0.91 than from 0.5 to 0.51. This is appropriate since a probability near either 0 or 1 represents near certainty.

3. *It is always well defined*: The distance metric should be defined for all the values of the two compared distributions.

As noted in Section 3.3.2, other distance metrics (e.g. KL divergence) that have been used in explanation, do not have all these properties. Another metric with these properties could be used instead of the Hellinger distance.

Threshold of Significance

The proposed approach for specifying the threshold of significance is an extension of INSITE's method. According to INSITE, the threshold θ is the minimum impact, so that:

$$E_i \in E_{sig} \text{ iff } \mathrm{Im}_E(E_i) \geq \theta \tag{7.3}$$

However, rather than giving θ directly, it is defined indirectly using a percentage of indifference α, where $0 \leq \alpha \leq 1$. First, a hypothetical posterior probability distribution G is defined. The distance from the posterior $P(T|E)$ to G is proportional of the distance from $P(T|E)$ to the prior $P(T)$, where G lies in the direction of change (Figure 7.3). Finally, θ is defined using the D_H between $P(T|E)$ and the hypothetical posterior G, such as:

$$G \triangleq P(T|E) - \alpha(P(T|E) - P(T)) \tag{7.4}$$

$$\theta \triangleq D_H(P(T|E)||G) \tag{7.5}$$

According to INSITE, the user can adjust the value of α until an acceptable range of indifference for $P(T|E)$ is found. An acceptable range of indifference means that changes outside that range are significant. This process gives the user the ability to adjust his expectation. However, this process can be time consuming. In addition, the user might not always be able to select the appropriate range of indifference. For these reasons, we propose a way of selecting the appropriate α, in which no input from the user is needed. In particular, we use a predefined set of decreasing $\alpha : \{\alpha_1 \dots \alpha_n\}$. Each percentage of indifference is used in turn to determine a threshold, continuing until at least half of the evidence variables E are included in E_{sig}.

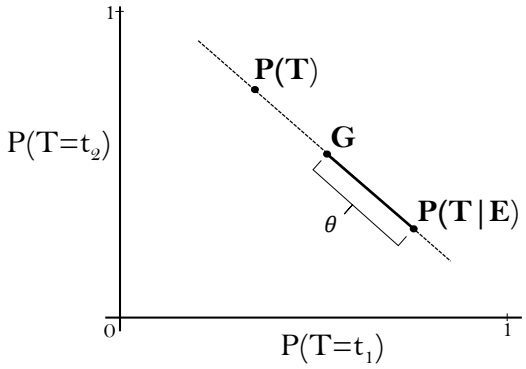

Figure 7.3: Threshold of significance for a binary target T (based on [254])

Identifying the set of significant evidence indirectly using a percentage of indifference α and not directly using θ, makes the process more generic. Firstly, the threshold θ relates to the applied distance measurement. To illustrate this, imagine that we have a BN with a binary target $T : \{t_1, t_2\}$ and a set E of 6 evidence variables $E : \{E_1 \dots E_6\}$. The prior, marginal posterior and posterior probabilities are: $P(T = t_1) = 0.097$, $P(T = t_1|E\backslash E_1) = 0.19$, $P(T = t_1|E\backslash E_2) = 0.15$, $P(T = t_1|E\backslash E_3) = 0.27$, $P(T = t_1|E\backslash E_4) = 0.11$, $P(T = t_1|E\backslash E_5) = 0.21$, $P(T = t_1|E\backslash E_6) = 0.26$, $P(T = t_1|E) = 0.2$. Using a predefined set $\alpha : \{0.5, 0.45, 0.4, 0.35, 0.3, 0.25, 0.2, 0.15, 0.1, 0.05, 0.01, 0.005, 0.001\}$ and applying the Hellinger distance we have $E_{sig} : \{E_4, E_3, E_2\}$ based on $\alpha = 0.5$ and $\theta = 0.049$. Applying the KL divergence, the set E_{sig} and the percentage α remain the same but the threshold of significance θ changes to 0.0045. In this example the same set of significant evidence was found in both scenarios based on the same α, but a very different θ. As a result, defining a set of θ directly becomes very hard, while using α makes the process more generic. In addition, θ also depends on the evidence scenario. In other words, the same distance metric and the same α can lead to very different θ in different scenarios. This is due to the

impact that each evidence variable has on the target. As a result, while directly choosing θ is possible, having an extra step of using a percentage of indifference α makes the process easier and more generic.

Conflict Analysis

Having identified the set of significant evidence variables E_{sig}, we next examine whether each evidence variable works in the same way in creating the overall change of T. This is known as 'conflict analysis' and we extend INSITE's method to work for variables with more than two states. When we perform a conflict analysis we compare (i) the direction of the change and (ii) the impact on the target when each evidence variable is removed with the impact when all the evidence variables are removed. The direction of change can be assessed using the difference $\Delta_t(E_i)$ for every state t of the target T and a member E_i of E_{sig}, such as:

$$\Delta_t(E_i) = P(t|E) - P(t|E \backslash E_i) \tag{7.6}$$

For each state t, the difference for an evidence variable $\Delta_t(E_i)$ is compared to the difference $\Delta_t(E) = P(t|E) - P(t)$. If both differences have the same sign for each state of T, then the direction of the change is consistent. If for each state of T the sign of those distances is the opposite, then the direction is conflicting. Finally, when the sign of the differences is not the same for each state of T, then the direction is mixed.

Imagine that we have the target B with three states b_1, b_2, b_3. Three probability distributions are shown in Figure 7.4. For the state b_1 the probability is consistently decreasing: $P(b_1|E) > P(b_1|E \backslash E_i) > P(b_1)$ and for b_3 it is consistently increasing, but b_2 changes in different directions. This is a mixed direction.

Based on the above rules, the definitions for the consistency with respect to the direction of change are:

$$d_{\text{cons}}(E_i, t) = \Delta_t(E_i) > 0 \Leftrightarrow \Delta_t(E) > 0 \tag{7.7}$$

$$d_{\text{conf}}(E_i, t) = \Delta_t(E_i) > 0 \Leftrightarrow \neg(\Delta_t(E) > 0) \tag{7.8}$$

$$D_{\text{consistent}}(E_i) = \forall t . d_{\text{cons}}(E_i, t) \tag{7.9}$$

$$D_{\text{conflicting}}(E_i) = \forall t.d_{\text{conf}}(E_i,t) \tag{7.10}$$

$$D_{\text{mixed}}(E_i) = \neg D_{\text{consistent}}(E_i) \wedge \neg D_{\text{conflicting}}(E_i) \tag{7.11}$$

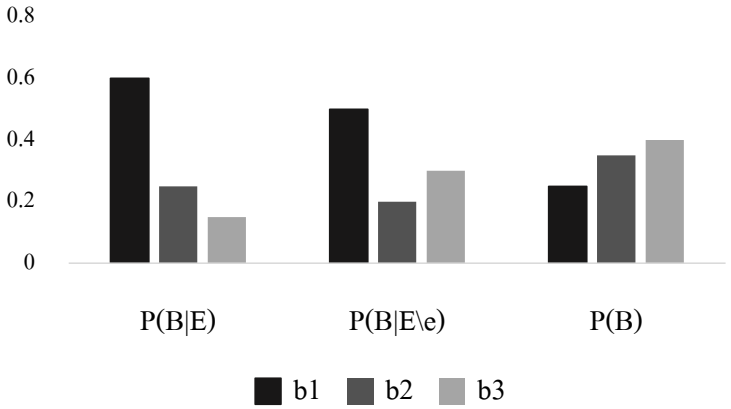

Figure 7.4: Example of Mixed Effects

The magnitude of the impact also needs to be considered. If all the evidence variables are working together, and the direction is consistent, the impact when one variable is unobserved is expected to be less than the impact when all the evidence variables are unobserved, such as $\text{Im}_E(E_i) \leq \text{Im}_E(E)$. However, it is also possible that removing the evidence E_i can lead to a greater impact than $\text{Im}_E(E)$, even though the direction is consistent. This suggest that E_i 'dominates' the remaining evidence. In case the direction of change is mixed, we can assess which effect is more significant using the Hellinger distance to compare the consistent with the conflicting part. Table 7.1 summarises the conflict categories.

Conflict Category	Direction	Impact
Dominant	$D_{consistent}$	$\text{Im}_E(E_i) > \text{Im}_E(E)$
Consistent	$D_{consistent}$	$\text{Im}_E(E_i) \leq \text{Im}_E(E)$
Conflicting	$D_{conflicting}$	n/a
Mixed consistent	D_{mixed}	$\text{Im}_E(E_i)_t \mid t \in d_{\text{cons}}(E_i,t) > \text{Im}_E(E_i)_t \mid t \in d_{\text{conf}}(E_i,t)$
Mixed conflicting	D_{mixed}	$\text{Im}_E(E_i)_t \mid t \in d_{\text{cons}}(E_i,t) \leq \text{Im}_E(E_i)_t \mid t \in d_{\text{conf}}(E_i,t)$

Table 7.1: Summary of the Conflict Analysis Categories

7.2.3 Level 2: Flow of Information

The second level of the explanation uses a simple approach to present the flow of reasoning from E_{sig} to T. First, a set of intermediate variables (X_I) is determined (Figure 7.5). The

Markov blanket variables (MB) of T are chosen as the potential set of X_I. In a BN, the MB of a variable shields it from the rest of the network and it consists of its parents, children and children's other parents (Figure 7.5a). From the MB variables we include in X_I only those that are unobserved (Figure 7.5b, 7.5c) and part of a d-connected path from E_{sig} to T, given the evidence variables E (Figure 7.5d).

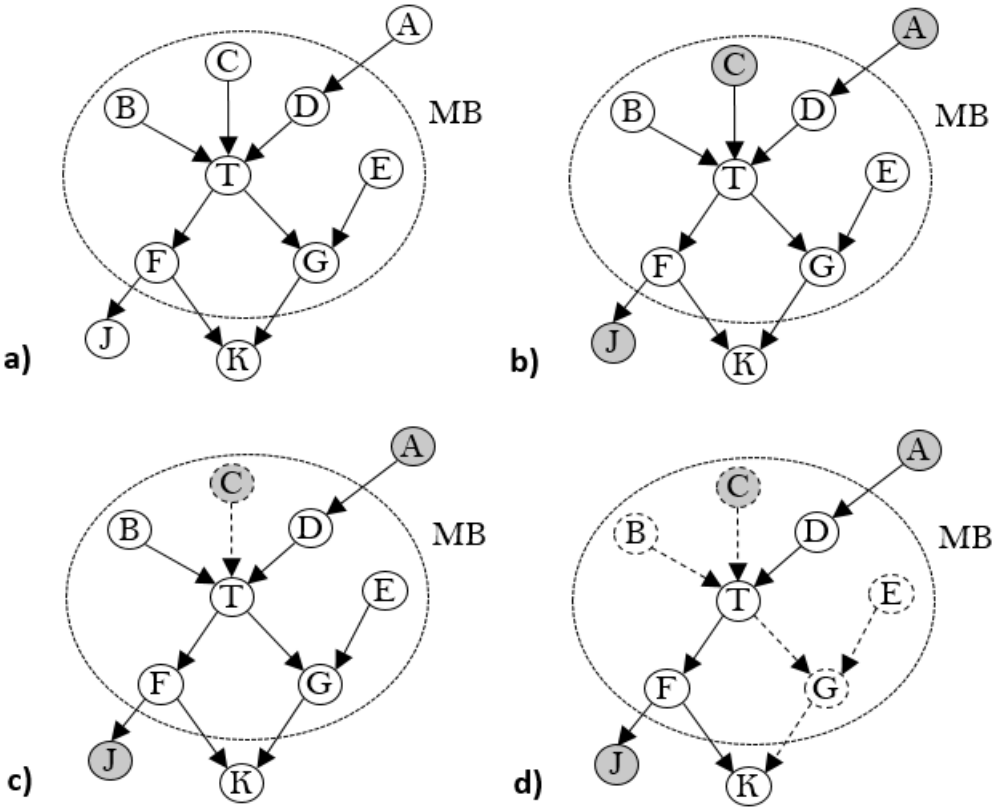

Figure 7.5: Process of finding the set of intermediate variables X_I. a) The MB of T is the set $\{B,C,D,E,F,G\}$. b) The variables A, C and J are observed. c) The variable C is observed, so it is excluded from the set of X_I d) The variables B, E and G are not part of a d-connected part from the evidence to T, so they are excluded from the set X_I, which is $\{D,F\}$.

In the second level of the explanation, the change in the uncertainty of each X_I is also shown. If the set X_I is empty (e.g. all the MB variables are observed), the explanation stops at the first level.

7.2.4 Level 3: Effect of Evidence on the Intermediate Variables

The final level of the explanation repeats some parts of the analysis of level 1 on the intermediate variables of level 2. For simplicity and consistency, we do not reassess the set of

E_{sig} for each X_I (Figure 7.2). Instead, for each variable in X_I, we first determine the subset of E_{sig} that are d-connected to them, and we carry out the conflict analysis as described in Section 7.2.2.

7.3 Case Study

In this section we use a real case study to show how the output of our method is translated into a verbal explanation. At the beginning, we give a brief description of the medical disease and the developed BN that is used as a case study.

7.3.1 Detecting Coagulopathy

In this case study, the developed BN was built to predict acute traumatic coagulopathy in the first 10 minutes of hospital care [282]. Coagulopathy is a bleeding disorder in which the blood's ability to clot is impaired. All the variables that may be observed within 10 minutes are shown in purple (Figure 7.6). The target variable, *COAGULOPATHY*, is shown in red. There are 11 variables in the MB of the target. The variables *PREHOSP* and *AGE* are observed, so they are excluded from the set of X_I. In addition, the variables *ROTEMA30* to *APTTr* (see top right) are not part of the flow of reasoning, while *DEATH* and *HEAD* are also not part of a d-connected path between the target and any of the evidence variables. As a result, only two intermediate variables, *ISS* (tissue Injury Severity Score) and *PERFUSION* (oxygen delivered to the tissues of the body), are available.

7.3.2 Verbal Output

The output of our algorithm is verbal and consists of three main parts: (i) numerical data, (ii) fixed text and (iii) dynamic text. Numerical data are presented using numbers. Fixed text consists of standard phrases that can be repeated in different scenarios and are presented with small letters. Dynamic text consists of the model's variables with their states and the change of their risk. Dynamic text is different in every scenario and is shown with capital letters. At the beginning, the prediction of the target is presented.

The likelihood of COAGULOPATHY = YES is 11%

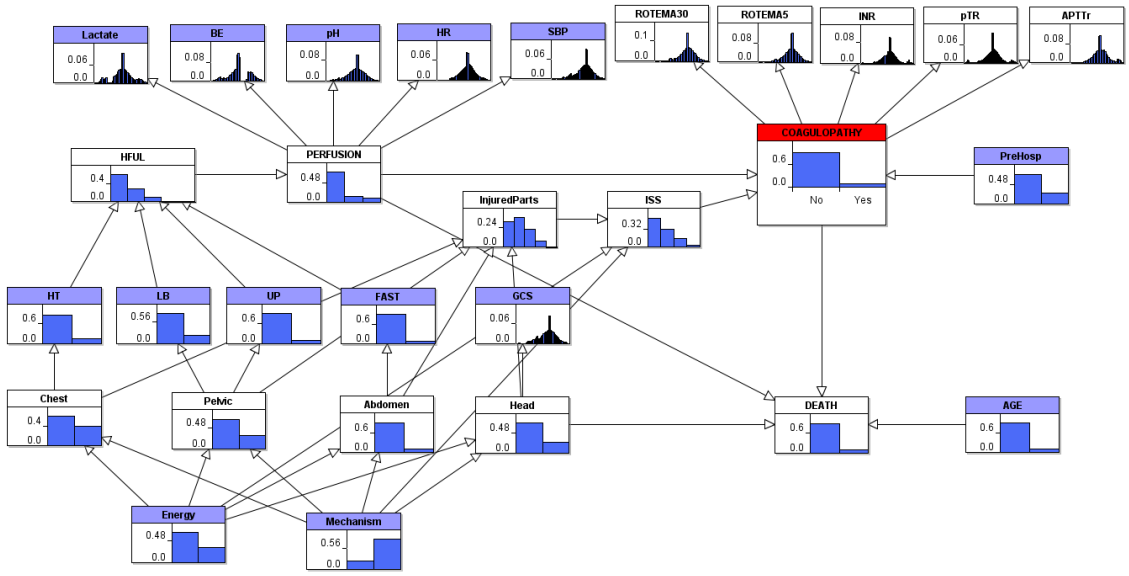

Figure 7.6: A BN model that predicts coagulopathy within 10 minutes of hospital care [282].

By default, the state with the highest probability is presented. In case the user wants to know the output of a specific state, he can configure it. In this case study, clinicians were interested only in the likelihood of having coagulopathy. Then, the first level of the explanation is illustrated. The supporting and conflicting significant evidence variables are presented in a decreasing order based on their significance. By default, the quantitative impact of each evidence is not presented as it makes the explanation unnecessarily complex for clinicians. In case the user wants to know the quantitative impact of each evidence, he can configure it. We can have up to four groups of significant evidence: (i) consistent and dominant evidence, (ii) conflicting evidence, (ii) mixed consisting evidence and (iv) mixed conflicting evidence (see Table 7.1)

Factors that support the INCREASED risk of COAGULOPATHY = YES (strongest to least):

- **PREHOSPITAL FLUIDS = 500mls (VERY IMPORTANT)**
- **GCS = 5 (VERY IMPORTANT)**
- **HAEMOTHORAX = YES (VERY IMPORTANT)**
- **ENERGY OF INJURY = HIGH**

Factors that do not support the INCREASED risk of COAGULOPATHY = YES (strongest to least):

- **SYSTOLIC BLOOD PRESSURE = 168**

- **LONG BONE FRACTURE = NO**
- **LACTATE = 0.9**

Coagulopathy is a binary variable, so no mixed effects are present. The significant evidence variables are described as 'supporting' or 'not supporting'. Supporting evidence is the consistent and dominant (distinguished by the phrase 'VERY IMPORTANT') variables as described in Section 7.2.3. Non-supporting variables are those classified as conflicting in Section 7.2.3. In this scenario, where the patient has an increased risk of becoming coagulopathic, compared to the average trauma patient (prior), the supporting evidence increases the risk (negative impact), while the non-supporting evidence decreases it (positive impact). Whether the supporting and non-supporting evidence has a positive or a negative impact on T is related to the scenario. Finally, the intermediate variables and their change are presented.

Important elements for predicting COAGULOPATHY are:

1. **PERFUSION: The likelihood of PERFUSION = NORMAL is 95%**
2. **ISS: The likelihood of ISS = SEVERE is 49%**

Level 2 shows how the intermediate variables X_I have been updated by the evidence. The likelihood of the state with the highest probability is presented. Again, the output of a specific state can be configured if needed. In the last level of the explanation we present the effect that the d-connected significant evidence variables have on each intermediate variable.

(1) Factors that support the INCREASED risk of PERFUSION = NORMAL:

- **SYSTOLIC BLOOD PRESSURE = 168**
- **LACTATE = 0.9**
- **LONG BONE FRACTURE = NO**

Factors that do not support the INCREASED risk of PERFUSION = NORMAL:

- **HAEMOTHOROAX = YES**

(2) Factors that partially support the INCREASED risk of ISS = SEVERE

- **GCS = 5**
- **HAEMOTHORAX = YES**

- **ENERGY OF INJURY = HIGH**
- **LONG BONE FRACTURE = NO**

Level 3 shows the impact that the significant evidence variables have on the intermediate variables. Since *PERFUSION* and *ISS* have more than two states, mixed effects can occur and, are presented with the terms 'partially support' and 'partially do not support'.

7.4 Evaluation

A small evaluation study was carried out with two aims: (i) compare the similarity between clinicians' reasoning and our explanation, (ii) examine the plausibility that the explanation can have a beneficial effect on clinical decision making. The model presented in Section 7.3.1 was used as a case study.

7.4.1 Study Design

In this study, we presented 10 cases to 16 clinicians (4 ED consultants, 4 trauma surgeons, 2 general surgeons, 2 ICU consultants and 4 general surgery specialist registrars). A group of clinicians reviewed each case and selected only those with an accurate prediction. The impact of an inaccurate prediction and its explanation on the decision making process was out of the scope of this study. More details about the selected cases can be found in APPENDIX F.

This was a before-after study split into two parts [255]. The first part helped us understand clinicians' reasoning and decision making. This was achieved by carrying out a baseline questionnaire (APPENDIX G) for each case (160 responses). The second part assessed the potential benefit of the explanation. Each clinician completed a follow-up questionnaire (APPENDIX H); for half of the cases only the prediction of the model was presented (*prediction* cluster: 80 responses) and for the other half an extra explanation of the model's reasoning was given (*explanation* cluster : 80 responses) (Table 7.2).

To control for biases, the cases in the two randomly created sets were matched pairwise based on their complexity. The same procedure was followed for the two random groups of consultants. The clinicians were matched in each group based on their expertise. Another factor that could cause bias was the order that each case was seen. For that reason, we

	Cases	
Clinicians	Set X	Set Y
Group A	*prediction*	*explanation*
Group B	*explanation*	*prediction*

Table 7.2: Each group of clinicians saw half of the cases only with the model's prediction (*prediction* cluster) and the other half with an extra explanation of the model's reasoning process (*explanation* cluster).

presented the *prediction* or the *explanation* cluster randomly to each clinician. Thus, we prevented any influence in the response with the model's explanation by their previous experience with only the prediction of the model and vice-versa.

7.4.2 Questionnaires

Each clinician completed a baseline (APPENDIX G) and a follow-up questionnaire (APPENDIX H). In each questionnaire the following questions were asked:

1. What is your initial impression of this case in relation to coagulopathy?
2. Why? Rank the available information from most important to least important
3. What would you do next?

On the follow-up questionnaires we also examined the potential benefit of the model's prediction. Only in the *explanation* cluster, we asked additional questions that rated how the extra information increased their trust on the model's prediction and how useful and clear it was.

7.4.3 Data Analysis

Two objectives were categorised as primary: (i) similarity between clinicians' reasoning and the explanation (*similarity*) and (ii) increase in trust in the model given an explanation (*trust*). The secondary objectives were: (i) potential benefit to the clinicians' assessment and decision making given an explanation (*potential benefit*) and (ii) clarity of the explanation (*clarity*).

To assess the *similarity*, we compared the evidence that they mentioned as significant with the evidence that our first level of the explanation was considered as significant. In particular, we defined 4 groups based on the percentage of the variables that were considered as significant by clinicians and were also part of the provided explanation. Thus, their qualitative answers were categorised into the following groups:

1. Not at all similar (clinicians' reasoning is 0% similar with the explanation)
2. Quite similar (clinicians' reasoning is $<$50% similar with the explanation)
3. Similar (clinicians' reasoning is 50 - 75% similar with the explanation)
4. Very similar (clinicians' reasoning is $>$75% similar with the explanation)

Imagine for instance that for a particular case, clinicians mentioned as significant the variables LB, UP, FAST, Lactate and the first level of the explanation has mentioned as significant the variables UP, Lactate, and GCS. As two out of the four variables mentioned by clinicians were also part of the explanation, the *similarity* belonged to group 3. As we focused on not missing any variable mentioned by the clinicians, no negative weight was given in cases that the explanation included more variables than those mentioned by the clinicians. The aim was to compare how similar is their reasoning and our explanation based on the same available evidence. As a result, only clinicians' reasoning in the baseline was examined.

Clinicians' *trust* in the model's prediction between the *prediction* and the *explanation* cluster was compared, using their answers to the seven-point scale question: 'How much would you say that you trust the prediction of the model?'.

The analysis of the *potential benefit* was based on three questions. First, we compared their assessment of coagulopathy not only in the baseline and the follow-up but also in the *prediction* and the *explanation* cluster. Then, based only on the follow-up questionnaires, we examined how useful the model was. The usefulness was two-fold: (i) confirmation of their assessment and (ii) revision of their assessment. Finally, we compared their baseline and follow-up answers on the question 'What would you do next?' to examine whether the extra information had an impact on their decision making process.

The *clarity* of the explanation was based on the final question of the *explanation* cluster 'How clear was the explanation of the prediction of coagulopathy?' and clinicians' feedback.

7.4.4 Results

We present the results in each of the 4 categories: *similarity*, *trust*, *potential benefit* and *clarity*.

Similarity

To assess the *similarity*, we tested whether the mean of the responses that were $\geq$50% similar (categories 3 and 4) with our explanation was greater than the mean of the responses that were $<$50% similar (categories 1 and 2) (0.71 vs 0.29). Based on a t-test (t = -8.3726), we had enough evidence to reject the null hypothesis and support our claim that the majority of clinicians' reasoning was $\geq$50% similar to our explanation (p-value < 0.001).

Trust

We wanted to test whether the number of clinicians who did not trust the model enough (scale 1-4) and those who trusted it (scale 5-7) were significantly changed between the *prediction* and the *explanation* cluster (Table 7.3). Each case was seen by a matched pair of clinicians (80 responses); one clinician has seen only the model's prediction (*prediction* cluster) and the other has seen also an explanation of the model's reasoning (*explanation* cluster). Based on McNemar's test we did not have enough evidence to reject the null hypothesis (p-value = 0.23).

		Prediction	
		Low trust [1-4]	High trust [5-7]
Explanation	Low trust [1-4]	1	16
	High trust [5-7]	9	54

Table 7.3: Counts of low and high trust in the *prediction* and the *explanation* cluster

Potential Benefit

The first element of the potential benefit that we investigated was whether there was any significant difference in their assessment of coagulopathy between the baseline and the follow up questionnaire. Wilcoxon matched-pairs signed-ranks test showed that we had enough evidence to reject the null hypothesis (p-value < 0.001) and support our claim. In addition, we examined whether for the coagulopathic patients, clinicians' assessment in the *explanation* cluster was greater that their assessment in the *prediction* cluster. Using the Wilcoxon matched-pairs signed-ranks test we had enough evidence to reject the null hypothesis (p-value = 0.048) and support our claim. Similarly, we tested whether clinicians' assessment for the non-coagulopathic patients was lower in the *explanation* cluster than the *prediction* cluster. However, we did not have enough evidence to reject the null hypothesis (p-value = 0.98).

Clinicians answered a seven-point scale question: 'How useful was the prediction of coagulopathy for confirming your assessment?'. We examined whether the number of clinicians that rated the model in the follow-up questionnaires as not very useful for confirming their assessment (scale 1-4) and those that rated the model as useful (scale 5-7) were significantly changed between the *prediction* and the *explanation* cluster (Table 7.4). There was no change between the two clusters.

		Prediction	
		Somewhat not useful [1-4]	Somewhat useful [5-7]
Explanation	Somewhat not useful [1-4]	12	18
	Somewhat useful [5-7]	18	32

Table 7.4: Counts of the usefulness in confirming their assessment in the *prediction* and the *explanation* cluster.

The same analysis was conducted about the usefulness of the model in revising their assessment (Table 7.5). Based on McNemar's test, there was not enough evidence to support a significant change between the *prediction* and the *explanation* cluster (p-value = 1.000). However, this came to a contradiction with our findings on clinicians' improved assessment given the explanation.

		Prediction	
		Somewhat not useful [1-4]	Somewhat useful [5-7]
Explanation	Somewhat not useful [1-4]	58	11
	Somewhat useful [5-7]	10	1

Table 7.5: Counts of the usefulness in revising their assessment in the *prediction* and the *explanation* cluster.

Finally, the extra information had no impact on their decision making process. In the baseline and the follow-up assessment their actions were the same.

Clarity

The clarity of the explanation was examined only in the *explanation* cluster (80 responses). We wanted to test whether the mean of those who rated the *explanation* as clear (states 5-7) is greater than the mean of those who did not find the explanation very clear (states 1-4). The t-test (t = -3.2455) between those two means (0.625 vs 0.375) showed that we had enough evidence to reject the null hypothesis (p-value < 0.001). Finally, in the *explanation* cluster clinicians gave their feedback on the explanation in an open question. Some of their comments were:

- *In the heat of battle, a colour coded guidance would aid clarity*
- *The words 'partially support' and 'partially do not support' are not very clear*
- *Why haemothorax (HT) at the beginning was very important and at level 3 was partially supporting*
- *Weighting leans towards more significant chance of coagulopathy*
- *Lactate 4.5 is non-supportive, 4.6 would be supportive?*
- *Level 1: useful brief explanation, level 3: too wordy*
- *ATC reassuring when agrees with my prediction*
- *Expected higher prediction*

7.5 Discussion

In this chapter, we have described a method that generates an explanation in three levels, each adding more details to the explanation. Our method can be applied to BNs with both discrete and continuous variables and requires no user input. It is suitable for real-time use even in large BNs, as it focuses on rapidly producing a good explanation and not necessarily the most complete one. Despite the benefit of having a quick and concise explanation, various restrictions have been accepted.

One major restriction in our method is the way we classify the evidence as influential. There are two quick approaches to identify the set of influential evidence: (i) observe each evidence variable in turn and compare the posterior probability with the prior (ii) remove each evidence variable in turn and compare the posterior with the posterior with all the evidence. Each approach focuses on a different type of influence, so each can miss detecting some influences under certain circumstances.

Imagine that we have a binary target T and two evidence variables A and B, that are parents of T. Two scenarios are available; (1) $P(T) = 0.9, P(T|A) = 0.23, P(T|B) = 0.21, P(T|A,B) = 0.41$, and (2) $P(T) = 0.9, P(T|\neg A) = 0.07, P(T|B) = 0.21, P(T|\neg A,B) = 0.17$. The variables T and B have the same state in both scenarios, while A is true in the first scenario and false in the second. If we use the approach (i) and compare the posterior when each evidence is instantiated (0.21 in both scenarios) with the prior (0.9 in both scenarios), the influence of B will be the same. This approach cannot distinguish between the two different scenarios, as it neglects the complete set of evidence. In comparison, the approach (ii) compares the posterior when B is temporally removed (0.23 in scenario (1) and 0.07 in scenario (2)) with the posterior when all the evidence variables are observed (0.41 in scenario (1) and 0.017 in scenario (2)), the influence of B is different in both scenarios.

Removing each evidence separately can distinguish different scenarios. However, there are situations, such as having OR or AND operator or mutually exclusive causes, where some influential evidence may be missed using approach (ii). Imagine that we have the AND operator, T is true if both A and B are true, with probabilities: $P(T) = 0.17, P(T|A) = 0.2, P(T|\neg B) = 0, P(T|A,\neg B) = 0$. Using approach (ii), A has a zero influence on T. Therefore, when we have the AND operator and at least one parent is false, using approach (ii)

we may miss some of the influential evidence. Similarly, when we have the OR operator and at least one parent is true. This problem becomes more important when we have more evidence. On the contrary, approach (i) gives a non-zero influence in both situations.

A combination of the two approaches would be more appropriate under certain conditions. However, we chose to use approach (ii) and remove each evidence, as it is crucial to account every time for the rest of the available evidence. This is closer to the real world and the way people think about explanation. We removed one evidence at a time and not combinations of the evidence to reduce the time to produce the explanation. We accept the risk of missing interactions since the time needed to search for the best combination of evidence increases exponentially when the model and the number of evidence variables become bigger. Further directions to overcome this limitation are mentioned in section 8.2.3.

The MB of the target is used as the intermediate step to capture the flow of information from the evidence to the target. The advantages of using the MB are: (1) every variable in a BN has a MB, so it can be generalised, (2) the MB of a variable contains important information about it, and (3) it can be used to produce a meaningful explanation very quickly. However, in large BNs, where the evidence is further from the target, important variables along the chain won't be captured in the explanation. We could overcome this limitation by adding another explanation level, if needed, in which we present the MB of the MB variables.

A small evaluation of the benefit of the explanation in clinical practice was conducted. This study was based only on 10 real cases, so it cannot give definitive conclusions. It was used as an initial pilot study to investigate the potential benefits and shortcomings of the explanation, and to teach us useful lessons for a future larger trial. This study primarily looked at the similarity between clinicians' reasoning and the generated explanation and at the increase in model's trustworthiness. Secondarily, we examined the potential benefit of the explanation on clinicians' decision making and assessment. Finally, the clarity of the explanation was tested.

The explanation produced by our method was similar to clinicians' reasoning; proving that our algorithm can produce a meaningful explanation. Clinicians trusted the model's prediction, but there was no significant change in their trust when an explanation was provided.

There was no impact on their decision making but there was a significant change in their assessment. They found the explanation useful for confirming their assessment, but not for revising it. However, there was not enough evidence to support a significant change when an explanation of the model's reasoning was given, which came to a contradiction with their improved assessment, especially for the coagulopathic patients. The explanation was found to be clear but very wordy by the majority of clinicians. They liked the first level of the explanation but found the third level of the explanation too complicated. They liked the idea of having an explanation but preferred it to be less wordy and potentially graphically enhanced.

Despite the sound design of the study, it had some limitations. A major limitation was the chosen cases, which were less uncertain. They had a degree of ambiguity because coagulopathy is an uncertain condition, but they were almost always similar with clinicians' expectations. That might explain why the explanation did not have a significant impact on the model's trust and clinicians' decision making. Coagulopathy is a disease that takes time to develop. When a trauma patient arrives in the ED there are some standard actions that clinicians could carry out, such as examine the patient, give blood, go to theatre, conduct extra imaging etc. Having a justified prediction of coagulopathy can reassure their beliefs but it is not going to make them change their decisions. This was potentially the reason why the explanation did not have a significant impact on their decision making. In addition, the chosen clinicians were very experienced, so probably a decision tool and an explanation have no significant benefit on their decision making. This can also justify the fact that they answered that the explanation was not very useful for confirming or revising their assessment, even if their assessment was significantly improved, especially for the coagulopathic patients. Finally, the length of the explanation could be an inhibiting factor.

Chapter 8

Summary and Future Directions

This chapter revisits the research hypotheses of this thesis and summarises the related contributions. The chapter ends with the future directions of research.

8.1 Research Hypotheses and Contributions

Many CDS BNs have been developed over the years, but a very small minority has been used in practice. In this thesis we tried to bridge the gap and we proposed practical ways for developing not only an accurate model but one that has the potential to be used and make a difference to clinical decision making. This research objective was investigated using three secondary objectives, related to (1) Support, (2) Assurance, and (3) Trust.

8.1.1 Support

Objective Capture the progress of an acute condition and the dynamic way in which clinicians gather information and take decisions with the potential to *support* clinical decision making for acute medical conditions in successive stages of the patient's care.

Knowledge Gap Many time-based BNs have been proposed to assist the dynamic nature of decision making. Despite their advantages, they are not applicable in many medical applications. An important limitation is time discretisation. Some methods either choose a fixed granularity, which is not always true in many medical problems, or they learn the granularity from data, which is not always in accordance with the process of clinical decision making. Another limitation is related to the way the structure and the parameters of the model are learned. Methods that have a stationary transition is too restricted in applications

where the clinical condition and the available information change over time. On the other hand, learning the structure and the parameters of the model merely from data in each time interval might not be possible, as medical datasets are not always complete enough and they cannot always reassure a causally coherent structure. More details on the knowledge gap can be found in Sections 2.6 and 3.2.

Contribution In Chapter 5, we proposed a method for developing a CDS BN that captures the rapid progression of an acute medical condition, the way clinicians gather information and take decisions in successive stages of the patient's care. The main characteristics of the proposed method are: (1) the BN structure is non-stationary, (2) the structure and parameters of the model are not restricted to the available data, and (3) the time interval between two stages of care is irregular, following clinicians' timeline and not data availability. In particular, the structure of the developed BN is based on expert's knowledge, which allows us to have a causally coherent structure. The parameters are learned primarily from data. Expert's knowledge is also used when no or not enough data were available. Our approach addresses some important research challenges. First, we propose a structured way of capturing and organising the necessary clinical knowledge. Then, we present a way of incrementally translating the elicited knowledge into a progressive BN. We particularly focus on how we can simplify the process of developing a complex BN structure. In addition, we show how we should model a treatment and how we can learn its parameters from observational data, avoiding the estimate being confounded by the non-random of the choice of treatments. Finally, we explain how we can train and validate the BN progressively, when different data sizes are available. The combat trauma care in the prehospital environment is used as a case study.

The methodology for developing a progressive BN can be applied to many acute conditions and it is not limited to the combat trauma care. In addition, the various challenges that Chapter 5 addresses are not specific to the case study. In many medical applications, data are not sufficient to provide a causal structure and experts are used instead. Our method explains which questions should be asked and how to organise the elicited clinical knowledge. In addition, dividing a big model into several submodels can be useful to other medical applications as well. Treatment variables are predominant in the majority of the medical BNs, therefore, our contribution on how to model a treatment and estimate its unconfounded effect can be useful. Finally, different data sizes in successive stages of care may be available

in other medical problems, as patients do not always follow the same clinical pathways. For instance, a patient that arrives in the ED can then go either to theatre for surgery, to the ICU ward or even been discharge to home.

8.1.2 Assurance

Objective Use a CDS BN as a healthcare governance tool to review and evaluate past treatment strategies to try to *assure* optimal future clinical decisions and clinical practice.

Knowledge Gap This objective was investigated in the specific clinical context of the DMS mortality and morbidity review meetings. During those meetings, the panel reviews the clinical practice using the medical and military notes and the available scoring systems. The current practice has some limitations. First, the scoring systems are simple mathematical scores that give a description of the injury severity at a specific time point. They cannot capture the progression of the soldier's condition as well as the consequences of the clinical practice. In addition, clinicians' ability to imagine alternative scenarios is not always optimal. More details on these limitations can be found in Sections 4.6.

Contribution In Chapter 6, we proposed an alternative use of the model developed in Chapter 5. In particular, we explained how we can use the developed BN, alongside the current practice, as an objective healthcare governance tool to answer counterfactual questions regarding alternative treatment decisions to assist the DMS mortality and morbidity review meetings. The method of twin networks helps us to represent the actual and the hypothetical clinical practice, where alternative treatment decisions are made. As far as we know this is the first time, where counterfactual reasoning is being proposed as a healthcare governance tool. In addition, we extend the use of counterfactual reasoning on progressive BNs to review clinical decisions, where the alternative treatment strategy and its effect belong to different stages of the patient's care.

Using three realistic categories of queries, we illustrate how the proposed counterfactual reasoning with BNs can be used to assist the DMS mortality and morbidity review meetings. Although, we used a military environment, this work can be easily extended to the civilian sector, as mortality and morbidity review meetings are conducted regularly there as well. Finally, the described approach for reviewing treatment decisions in a progressive BN can be applied to other time-based BNs, where treatments are part of the model's structure.

8.1.3 Trust

Objective Make the model's reasoning clearer to clinicians to increase their *trust* in the model and the chances of using it.

Knowledge Gap Several approaches have been proposed to explain the reasoning of a BN. However, there are many situations where these methods cannot be applied. First, most of the existing methods can be applied to BNs that include only discrete variables. Some are even restricted to binary variables only. However, most of the medical BNs include continuous nodes as well. In addition, most of the methods try to find the best explanation that can be time-consuming, especially for large BNs, which are common in medical applications. Finally, the user's input is often required in different stages of the explanation. This can be problematic, especially in situation where there is a time pressure. More details on the limitations can be found in Section 3.3.3.

Contribution In Chapter 7, we proposed a practical method of explaining the reasoning in a BN, so that the user can understand how a prediction is generated. The proposed method can be used in hybrid networks that have both continuous and discrete nodes and requires no user input. In addition, we simplify the process of identifying the most important evidence and chains of reasoning, so we can be able to produce rapidly a good and concise explanation, but not necessarily the most complete one. Our method produces an incremental explanation that has three successive levels of detail. The key questions that we answer are: (1) which important evidence supports or contradicts the prediction, and (2) through which intermediate variables does the information flow.

A BN developed by others to provide decision support in treating acute traumatic coagulopathy for injured civilians in the ED is used as a case study. A small evaluation study is conducted as well. This study shows that the proposed method can produce a meaningful explanation that is consistent with clinicians' reasoning. Even though the explanation is found clear and has an impact on their assessment, there is not enough evidence to support a significant change in clinicians' trust and decision making. As explained in Section 7.5, this might be because of the selected cases and the clinicians chosen. Although, our approach has been applied and tested only in a specific BN, we believe that it can be applied to other BNs with similar characteristics.

8.2 Future Directions

The novel contributions explained in this thesis suggest many possible future directions. Below we present some interesting future directions for each secondary research objective.

8.2.1 Support

The systematic way of capturing experts' knowledge proposed in Chapter 5 could be extended to the development of care maps. A care map could combine expert's knowledge and clinical guidelines to present all the possible clinical pathways. At each stage of the pathway information such as diagnostic tests, symptoms, and clinical practice will be captured. The produced care map could then be used to develop the BN structure. Despite the incremental approach proposed in Chapter 5 and the existing structured approaches, such as Object Oriented BNs, a better approach is needed to build a BN with several levels of abstraction. This is especially true in situations when we want to combine real time data from local sensors with background data. Moreover, the progressive BN proposed in Chapter 5 can model only successive stages of care. In cases, there is a loop among the stages of care or some stages along the way are avoided or chosen under certain circumstances, it would be useful to combine the method of a progressive BN with the advantages of a gated BN [21]. Finally, a frequent question is "How much data are enough to learn the true relationships in the BN?". A common answer is the more the better. It is not easy to give a clear answer as the data size depends on the complexity of the model and the number of the parameters that should be learned. However, it would be useful to be able to identify which part of the model is more complex and requires more attention, such as additional data or published evidence or even expert judgement.

8.2.2 Assurance

The work presented in Chapter 6 is a first attempt to explain the usefulness of extending the use of counterfactual reasoning as a healthcare governance tool to review past treatment decisions. Many useful future directions exist. Counterfactual reasoning using a BN is a controversial area. Making clinicians believe that counterfactual reasoning with BNs is an accurate process will not be an easy task. Using real cases, we should explore how counterfactual reasoning with BNs can be presented and explained to clinicians and be integrated into the existing process of the DMS mortality and morbidity review meetings. In addition,

developing an automate way to create twin networks will help us to perform counterfactual reasoning to many cases and investigate whether we can detect suboptimal treatment strategies. Moreover, it would be beneficial to study the impact that counterfactual reasoning with BNs has on various aspects of clinical practice, such as identifying medical negligence, reporting medical mishaps, and learning from past mistakes. Apart from the described future steps of counterfactual reasoning with BNs related to the case study, there are some future methodological directions as well. First, it would be useful to investigate how we can perform counterfactual reasoning with BNs when multiple decisions are reviewed at the same time. Another interesting research topic would be to investigate whether the accuracy of the BN that represents the actual world is enough to reassure an accurate BN in the counterfactual world.

8.2.3 Trust

In Chapter 7, we proposed a quick way to generate a concise explanation of reasoning for BNs that contain both discrete and continuous nodes, without any further input from the user. To reduce the time to search for the best combination of evidence, only one item of evidence was removed at a time. As explained in Section 7.5, this restriction may miss detecting some important evidence under certain circumstances. In addition, for saving time we only used the MB of the target as the intermediate step in the reasoning process. This can help us to generate a meaningful explanation quickly, but important information, especially in large BNs, might be missed. A useful next step is to investigate how we can prune the available evidence and intermediate variables, using the knowledge of the model's structure and the domain knowledge. For instance, it would be useful to generate an explanation by making use of abstract semantics, such as idioms. In addition, the proposed method targets only BNs that are used as a one-time activity. A useful extension would be to investigate how our explanation can be extended to progressive and time-based BNs, where the explanation generated for a target in a later stage should distinguish between evidence entered in the same stage and in earlier stages. An enhanced graphical representation and an evaluation of the explanation in real time would help us to examine how much a decision maker makes use of the explanation under real conditions and potentially time pressure. Another future step is to try and combine the explanation of the model's reasoning with other types of explanation such as the explanation of the model and/ or the explanation of the evidence 3.3.1. The explanation of the model's reasoning could benefit also the methods

proposed in Chapters 5 and 6. An explanation of the model's reasoning could be used to identify which part of the BN's structure is incorrect. An inconsistent explanation might be the result of a wrong structure. Finally, an explanation could also be used to explain and compare the actual with the counterfactual world to make counterfactual reasoning more trustworthy.

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Appendix A

JTTR form

RESTRICTED – MEDICAL (when completed)

Trauma Audit Form Version 5.2 Oct. 2011 ☐Scored ☐Database ☐Completed	DB No.

DEPLOYED TNCs

USE THIS FORM FOR

- **ALL** Patients who have been the subject of a Trauma Call
- **ANY** UK Service person who is to be evacuated to RCDM for in-patient care following a traumatic injury – (Hostile or Non-Hostile)

DEMOGRAPHICS	Op Theatre Medical Treatment Facility If other, state: Role of MTF 3	Country Region City

Force	Supplying Country	Designation	
Regt/Corps	Service No.	Rank	Gender
Surname	First Name	DOB	Age
	F/Med 830 No.	Trust ID	

INJURY	Date of injury Time hrs	Scoring Cat:	Environment Military Intent

Injury Type: ☐Blast ☐Blunt ☐Penetrating ☐Thermal ☐Other	☐ Blast Exposure Suspected
Mechanism of Injury	Location of Incident
Trapped: How Long min	Circumstances of Injury

Body Armour	more more		
	If other, state:	Visibly Damaged	☐
Helmet	If other, state:	Visibly Damaged	☐
Eye Protection	If other, state:	Visibly Damaged	☐
Genital Protection	If other, state:	Visibly Damaged	☐
Hearing Protection	If other, state:	Visibly Damaged	☐
Gloves	If other, state:	Visibly Damaged	☐

Localisation of Victim When Injured

Vehicle Information

Vehicle more more If other, state:

Location Restraint

Environmental Information

Temperature (°C) Humidity (%) Rain Snow Altitude (m) CBRN Information

Brief incident history *(including any delay in evacuation with reason)*:

PRE-HOSPITAL / ROLE 1

Unit providing treatment:

Nationality of Unit:

Time at scene Time left scene

Treatment by: ☐MO ☐Nurse ☐Paramedic ☐CMT/MA ☐Team Medic ☐Buddy ☐Other (state)

Triage Category

Interventions:

Airway #1 Airway #2

Airway #3 Airway #4

Airway #5 Airway #6

Airway #7 Airway #8

☐ Airway Obstruction ☐ Extraction of object in the mouth: Time

☐ Asherman Chest Seal: Time ☐ Bolin Chest Seal: Time

☐Needle Decompression: Time ☐Was tension pneumothorax present?

ICD: ☐L ☐R ☐Thoracostomy: Time ☐Thoracotomy: Time

☐Morphine ☐IV mg ☐IM mg

Access: ☐IV ☐Central IO

☐CPR: Start Time End Time

Spinal Immobilisation: ☐Collar ☐Head blocks ☐Long board

Limb traction: ☐Sager splint ☐Box splint ☐Neoprene splint ☐Sam splint

☐Sam Pelvic sling Other Splint

Exposure Intervention: ☐ Blizzard blanket Other

Vitals: GCS Total / 15

E /4 V /5 M /6

AVPU A☐ V☐ P☐ U☐

BP / mmHg

Capillary Refill Time (secs)

Pulse Rate ☐Radial ☐Femoral ☐Carotid

Resp Rate

SPO2 % Temp °C

Pain score before

Pain score after

Pupil reaction (left) Pupil size (left)

Pupil reaction (right) Pupil size (right)

Haemorrhage: ☐ Active Bleeding: Time ☐ rFVIIa: Time ☐ Celox Gauze: Time

☐ FFD: Time ☐ Compressive Dressing: Time

1st Tourniquet applied to Time applied Time released

2nd Tourniquet applied to Time applied Time released

3rd Tourniquet applied to Time applied Time released

4th Tourniquet applied to Time applied Time released

Pre-Hospital drugs

Drug Name	Dose	Route

Pre-Hospital fluids (enter blood products later):

Fluid Name	Volume
	mls
	mls
	mls
	mls
	mls
	mls
	mls
	mls
	mls

MERT / BLM	Unit providing treatment: Nationality of Unit:

Transport: (If other, state:)	Time at scene Time left scene
Vehicle wheels – tracked ☐	Adverse events during transport:
Medical material on vehicle: ☐ Oxygen ☐ Mattress	

Treatment by: ☐MO ☐Nurse ☐Paramedic ☐CMT/MA ☐Team Medic ☐Buddy ☐Other (state)

Interventions: (GCS prior)	Vitals: GCS Total / 15
Airway #1 Airway #2	E /4 V /5 M /6
Airway #3 Airway #4	AVPU A☐ V☐ P☐ U☐
Airway #5 Airway #6	BP / mmHg
Airway #7 Airway #8	Pulse Rate ☐Radial
☐ Extraction of object in the mouth: Time	☐Femoral
☐ Asherman Chest Seal: Time ☐ Bolin Chest Seal: Time	☐Carotid
☐Needle Decompression: Time ☐Was tension pneumothorax present?	
ICD: ☐L ☐R ☐Thoracostomy: Time ☐Thoracotomy: Time	
Access: ☐IV ☐Central IO	Resp Rate
	SPO2 % Temp °C
☐CPR: Start Time End Time	Pain score before
Spinal Immobilisation: ☐Collar ☐Head blocks ☐Long board	Pain score after
Limb traction: ☐ Sager splint ☐Box splint ☐Neoprene splint ☐Sam splint	
☐Sam Pelvic sling Other Splint	

Pupil reaction (left) Pupil size (left)
Pupil reaction (right) Pupil size (right)

Haemorrhage: ☐rFVIIa: Time ☐ Celox Gauze: Time ☐ FFD: Time
☐ Compressive Dressing: Time
1st Tourniquet applied to Time applied Time released
2nd Tourniquet applied to Time applied Time released
3rd Tourniquet applied to Time applied Time released
4th Tourniquet applied to Time applied Time released

In-transit drugs

Drug Name	Dose	Route

In-transit fluids (enter blood products later):

Fluid Name	Volume
	mls
	mls
	mls
	mls
	mls
	mls
	mls
	mls
	mls

FD HOSPITAL RESUS	Date	Time	Trauma Team Called ☐Yes ☐No
Trauma Team Leader:		Reason for Trauma Call:	☐Right Turn

Triage Category on Arrival

Interventions: (GCS prior)

☐Surgical Instrument Applied: Time

Airway #1 Airway #2

Airway #3 Airway #4

Airway #5 Airway #6

Airway #7 Airway #8

☐ Extraction of object in the mouth: Time

☐Needle Decompression: Time ☐ Was tension pneumothorax present?

ICD: ☐L ☐R ☐Thoracostomy: Time ☐Thoracotomy: Time

Access: ☐IV ☐Central IO

☐CPR: Start Time End Time

Spinal Immobilisation: ☐Collar ☐Head blocks ☐Long board

Limb traction: ☐ Sager splint ☐Box splint ☐Neoprene splint ☐Sam splint

☐Sam Pelvic sling Other Splint

Vitals: GCS Total / 15

E /4 V /5 M /6

BP / mmHg

Pulse Rate

Resp Rate

SPO2 % Temp °C

Pain score on arrival ED

Pain score depart ED

White cell count

Pupil reaction (left) Pupil size (left)

Pupil reaction (right) Pupil size (right)

Haemorrhage: ☐ Celox Gauze: Time ☐ Compressive Dressing: Time

1st Tourniquet applied to Time applied Time released

2nd Tourniquet applied to Time applied Time released

3rd Tourniquet applied to Time applied Time released

4th Tourniquet applied to Time applied Time released

rFVIIa (complete the following if administered)

1st dose	mg	Time	Temp.	pH	PO_2	PCO_2	BE	Where
2nd dose	mg	Time	Temp.	pH	PO_2	PCO_2	BE	Where

☐ Massive transfusion protocol initiated

☐CT: Time

☐Head ☐Chest ☐Abdo ☐Pelvis ☐Limbs

☐C Spine ☐T Spine ☐L Spine

☐FAST US: Time

X-Ray: Time

☐Skull ☐Chest ☐Abdo ☐Pelvis ☐Limbs

☐Spine

FD Hospital Resus Drugs

Drug Name	Dose	Route	Length of course of treatment

Total fluids given during ED resus

Fluid Name	Volume
Total Crystalloids-Isotonic given	mls
Total Colloids given	mls
Total fluids given during Immediate Surgery	
Total Crystalloids-Isotonic given	mls
Total Colloids given	mls

				Other fluids given	
					mls
					mls
					mls
					mls
					mls

Total Blood products given (units)

	Blood(RCC)	FFP	Cryo	Platelets	Emergency Donor Panel		
					Whole Blood	Platelets	
Role1							
MERT							
Resus							
Initial Theatre							
Other							
Total							

Disposal: ☐Ward ☐Surgery ☐ITU/HDU ☐Mortuary ☐RTU ☐External Transfer ☐Unknown

Disposal Date: **Time:**

Progress Notes:

Red Cross Wound Classification: Classify the 2 most serious injuries prior to surgery and in conjunction with surgical opinion, refer to explanatory notes							
Injury No.	**E**	**X**	**C**	**F**	**V**	**M**	**G**
Injury No. below	**E**	**X**	**C**	**F**	**V**	**M**	**G**

	Date	**Injuries**	**AIS 05 Code**
1			
2			
3			
4			
5			
6			
7			
8			
9			
10			
11			
12			

ISS	**NISS**	**RTS**	**TRISS**	**ASCOT**

OPERATIONS PERFORMED **Surgeon(s):**

	Date	Procedure:	Commenced	Finished	Lowest & Highest Temp
1					/
2					/
3					/
4					/
5					/
6					/

Performance Indicators appropriate to patient pathway ☐**Pre-Hospital** ☐**ED** ☐**Theatre** ☐**Critical Care** ☐**Ward** ☐**Burns**
Tick those areas where the patient has been treated and record the appropriate performance indicators by speaking to staff in those areas.

☐ KIA ☐ DOW ☐ WIA ☐ KNEA ☐ DNEA ☐ WNEA

're-Hospital Care Performance Indicators	Yes	No	NA	Comments
ime from point of wounding to BATLS skills <1 hour?	☐	☐	☐	
ime from point of wounding to *appropriate* surgical care <2 hours?	☐	☐	☐	
/ fluid boluses given to maintain radial pulse?	☐	☐	☐	
CS measured prior to intubation?	☐	☐	☐	
/as ETCO2 measured if the patient was intubated?	☐	☐	☐	
ypothermia mitigation equipment used where appropriate?	☐	☐	☐	
ull spinal immobilisation used where appropriate?	☐	☐	☐	
ital signs recorded to a minimum standard (RR, SpO2, PR, radial pulse present, AVPU, pain score)?	☐	☐	☐	
ain score <3 after analgesia.	☐	☐	☐	
id the patient receive antibiotics within 1 hour of wounding?	☐	☐	☐	
ong bone fractures stabilised <1 hour of injury?	☐	☐	☐	
IIST handover performed at the ED?	☐	☐	☐	
:mergency Department Performance Indicators	**Yes**	**No**	**NA**	**Comments**
emperature >36°C on arrival?	☐	☐	☐	
ital signs recorded on arrival (minimum data: RR, SPO2, BP, PR, GCS, pain score, blood gases, BM Stix)?	☐	☐	☐	
epeat vital signs recorded every 10 minutes in 1st hour (minimum data: RR, SPO2, BP, PR, GCS, pain core)?	☐	☐	☐	
CS <9 - RSI/ETT completed within 10 minutes of arrival in ED?	☐	☐	☐	
TCO2 recorded every 10 minutes in all patients ventilated in ED?	☐	☐	☐	
mergency thoracotomy for patients in extremis <10 minutes of arrival in the ED?	☐	☐	☐	
urgical airway secured (if required) within 10 minutes of arrival in the ED?	☐	☐	☐	
CS <9 with isolated closed head injury - CT head performed <1 hour minutes arrival?	☐	☐	☐	
enetrating extremity wounds x-rayed pre-debridement?	☐	☐	☐	
etadine soaked dressing applied to wounds within 1 hour of arrival in ED?	☐	☐	☐	
etanus IgG given in heavily contaminated wounds within 4 hours of arrival in ED?	☐	☐	☐	
ıdications for novel haemostatic use clearly documented?	☐	☐	☐	
ourniquet (if used) reviewed by a surgeon within 2 hours of application?	☐	☐	☐	
ain score maintained at 2 or below?	☐	☐	☐	
K measured for crush and burns patients and/or when CAT applied for above 1 hour?	☐	☐	☐	
'heatre Performance Indicators	**Yes**	**No**	**NA**	**Comments**
enetrating abdominal injury with BP <90 Systolic undergo laparotomy <30 minutes from arrival in ED?	☐	☐	☐	
rgent thoracotomy performed for shocked patients with penetrating chest injury <1 hour of arrival in the ED?	☐	☐	☐	
asualties with continuing haemorrhage with shock taken to theatre <30 minutes from arrival in ED?	☐	☐	☐	
amage control laparotomy (if performed) performed in <90 minutes from ED arrival?	☐	☐	☐	
/as the laparotomy if performed therapeutic?	☐	☐	☐	
asciotomies performed for confirmed vascular injuries?	☐	☐	☐	
cute compartment fasciotomies performed <1 hour of arrival in ED?	☐	☐	☐	
evascularisation surgery performed <6 hours of injury?	☐	☐	☐	
ecompressive craniotomy/craniectomy performed <4 hours of a blunt head injury?	☐	☐	☐	
losure of penetrating head injuries performed <6 hours of injury?	☐	☐	☐	
ll wounds photographed pre and post debridement with copies available in UK?	☐	☐	☐	
ll wounds ICRC scored at initial surgery?	☐	☐	☐	
imb salvage scoring performed pre amputation (2 surgeon agreement)?	☐	☐	☐	
ppropriate initial wound surgery performed <6 hours of injury?	☐	☐	☐	
acteriological specimens taken pre and post each debridement with results available to clinicians?	☐	☐	☐	
ppropriate antibiotics commenced within 6 hours of open fracture?	☐	☐	☐	
ff table temperature >34°C?	☐	☐	☐	
utritional assessment plan documented post surgery?	☐	☐	☐	

ritical Care Performance Indicators	Yes	No	NA	Comments
linimum monitoring standards followed during anaesthesia?	☐	☐	☐	
b maintained >8 g/dL during hospital admission and AEROMED?	☐	☐	☐	
lycaemic level 4-8mmol/L sustained during admission and AEROMED?	☐	☐	☐	
0 degree head up maintained on ITU & during AEROMED (ventilated patient)?	☐	☐	☐	
U patients evacuated within 48 hours of admission to ITU?	☐	☐	☐	
ost-operative period Performance Indicators	**Yes**	**No**	**NA**	**Comments**
o CSF leak post neurosurgery?	☐	☐	☐	
o missed penetrating/sight threatening ocular injury?	☐	☐	☐	
o missed eardrum injury?	☐	☐	☐	
o unplanned re-laparotomies or re-thoracotomies?	☐	☐	☐	
o unplanned admission to critical care?	☐	☐	☐	
ost operative temperature maintained > 34°C?	☐	☐	☐	
ull tertiary survey (including spine) carried out <24 hours of arrival in ED?	☐	☐	☐	
MWH started within 24 hours of admission?	☐	☐	☐	
ED stockings fitted?	☐	☐	☐	
Vard Performance Indicators	**Yes**	**No**	**NA**	**Comments**
/aterlow score performed on admission to ward?	☐	☐	☐	
ollow-up Performance Indicators	**Yes**	**No**	**NA**	**Comments**
ase discussed at a weekly MDT meeting?	☐	☐	☐	
ignificant events fed back to the theatre of operation?	☐	☐	☐	
ase discussed at a 6 monthly morbidity and mortality meeting?	☐	☐	☐	
urns Performance Indicators	**Yes**	**No**	**NA**	**Comments**
SA, location, depth estimate and fluid resuscitation begun <1 hour of burn?	☐	☐	☐	
halation/airway injury identified <1 hour following burn?	☐	☐	☐	
ormal burn assessment (dressing and accurate fluid resuscitation) performed <4 hours following burn?	☐	☐	☐	
mb escharotomy within <4 hours of burn?	☐	☐	☐	
G feeding begun within 6 hours of burns >15% BSA?	☐	☐	☐	

COMPLICATIONS	Were there any complications yes/no/unknown (see complication list)		
	Date/Time	**Details**	**Code**
Pre Hospital			
Airway			
Fluids			
Miscellaneous			
Hospital			
Airway			
Pulmonary			
Cardiovascular			
GIT			
Hepatic			
Haematological			
Infection			
Renal / GU			
Musculoskeletal			
Neurological			
Vascular			
Ophthalmology			
Psychiatric			
Other			
Provider			

DISCHARGE / TRACKING	Aeromed Priority ☐P1 ☐P2 ☐P3 ☐CCAST ☐N/A		
Date Admitted	**Location**	**Date Discharged / Transferred**	**Length of stay (days)**

On Completion of this form please return to: Trauma Nurse Coordinator, Academic Department of Military Emergency Medicine, Royal Centre for Defence, Medicine Institute of Research And Development, Birmingham Research Park, Vincent Drive, Edgbaston, Birmingham, B15 2SQ.

Appendix B

MERT form

PROTECT – MEDICAL (when completed)

Annex A to
ASOP 1
Dated 1 Nov 10

UK DEFENCE MEDICAL SERVICES PREHOSPITAL REPORT FORM (MERT) REV NOV 10

Team: Physician:		**Paramedic:**		**Nurse:**		**Fourth/Paramedic:**
Name:		Date: / /		Nationality/Service/Unit:		**PRF No:**
Sex: M / F	Age:	DOB: / /		Service No / Rank:	Location:	
Incident time: : (L)		Call time: : (L)		Deployed time: : (L)	On-Scene: : (L)	Off-Scene: : (L)
Pre-Hospital factors:	MIST Y/N 9-liner Y/N	Secure HLS Y / N		Hold Y / N Delay in launch		

Pre-Hospital **Free Text:** CAT (Times:)

M:
I:
S:
T:

Mechanism

❑ IED (Circle as appropriate) PP/ED/CW/ED/SB/ED/VB/ED Dismounted/Mounted Vehicle Type:

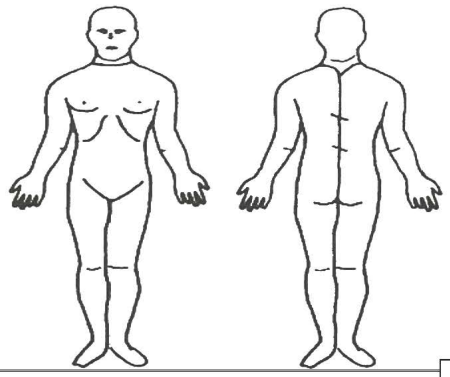
❑ Mines ❑ GSW ❑ IDF ❑ Fragments (RPG/Airburst) ❑ Burns ❑ Fall ht. [m] ❑ Other Battle Injury state: [ ]

❑ MVC/IED Mounted ❑ Driver ❑ Ejected ❑ Rear Seat ❑ Top Cover ❑ Rollover ❑ Wearing Seat Belt ❑ Trapped duration [ ]

❑ Body Armour Type: Osprey Version: CBA: ❑ Helmet Type: Mk6a/Mk7 ❑ Ballistic Goggles

DNBI (Insert Diagnosis): Surgical: Medical: Orthopaedic: Environmental/Other:

INJURIES:



Indicate motor/sensory level by shading

Free Text

Time Life Pronounced Extinct

Primary Survey **Pt Name** **PRF No:**

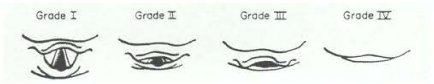
PROTECT – MEDICAL (when completed)

Cat Haemorrhage: Y / N ❑ C.A.T Time:[ ] Site: [ ] ❑ C.A.T Time:[ ] Site: [ ] ❑ C.A.T Time:[ ] Site: [ ]
❑ Haemostatic Agent Type: [ ] Time:[ ] Sites:[ ] ❑ FFD Sites: [ ] No: [ ]

Airway: ❑ Clear ❑ Obstructed ❑ Suction ❑ OPA Size: [ ] ❑ NPA Size: [ ]
❑ RSI (Document Below) Indication:
❑ Surgical Airway ❑ Type ❑ Size Indication:

C-Spine: ❑ Manual Immobilisation ❑ Collar ❑ Head Blocks ❑ Spinal Board ❑ Not Tolerated

Airway RSI (Drugs used documented above) ❑ Intubated Pre-MERT
❑ Pre-O_2 with BVM ❑Cricoid Pressure ❑Blade Size: Mac 2 3 4 ❑Airtraq
❑ETT Size [ ] ❑ Cuffed ❑ Uncuffed ❑ Bougie ❑ Stylet



❑ Airway soiled ❑ No of attempts: ❑ EasiCap ❑ Oesophageal Intubation Detector ❑ $ETCO_2$
❑ Bilateral chest expansion ❑ Tube tie ❑ Tape ❑ Thomas ETT holder

Free Text

Breathing: ❑ Normal ❑ Difficulty ❑ No Spont Resps ❑ BVM required ❑ Oxygen (15 L/min)
Bolin: ❑ L ❑ R Needle Decompression ❑ L ❑ R
Chest-drain: ❑ L ❑ R Thoracostomy : ❑ L ❑ R ❑ Thoracotomy Indication:

Circulation: ❑ ext. bleed Site [ ] ❑ Int. Bleed Location: [❑ Chest ❑ Abdo ❑ Pelvis ❑ Femur]
❑ Radial pulse ❑ Femoral Pulse ❑ Carotid Pulse ❑ No Pulse ❑ CPR Pre-MERT Y/N Time Commenced:
❑ IV /I O Site: [ ] Size: [ ]
❑ IV /I O Site: [ ] Size: [ ]
❑ IV /I O Site: [ ] Size: [ ] ❑ Pelvic Sling

Disability: A V P U GCS Total: (E= V= M=) ❑ Pupils equal ❑ Unequal: R [ ] L [ ] Reactive: ❑L ❑R Posture:

Exposure: Log Roll: Y / N Temp: Cold / Hot / Normal Blizzard: Y / N

Obs (time)							**Drugs**	**Route**	**Dose**	**Time**	**Signature**
HR (/min)											
RR (/Min)											
BP (mmHg)											
SpO_2 (%)											
GCS / AVPU:											
Pupils											
$ETCO_2$											
Pain Score/3											

BLOOD AND IV FLUIDS

Fluid	**Start**	**Finish**	**Signed**		**Fluid**	**Start**	**Finish**	**Signed**
1				5				
2				6				
3				7				
4				8				

H/O Time :	**Triage Category: (Circle)** T1 T2 T3 D	**Disposal:** Hospital: [ ] Hospital No:	**Disposal** ❑ ED ❑ Theatre ❑ Mortuary	**MERT Aircraft Type**

Completed by:	Name:	Rank:	Signature:	Clinical Lead:	Initials

Appendix C

Variables' description of the progressive BN developed in Chapter 5

Variable Name	Variable Description	Variable States	Variable Dynamics	Variable Types
MOI	Mechanism of injury	{Penetrating, Blast}	Fixed (Field Care)	Other
Chest Injury	Severity of chest injury	{None, Mild, Moderate, Severe}	Fixed (Field Care)	Other
Abdominal Injury	Severity of abdominal injury	{None, Mild, Moderate, Severe}	Fixed (Field Care)	Other
Pelvic Injury	Severity of pelvic injury	{None, Mild, Moderate, Severe}	Fixed (Field Care)	Other
Limb Injury	Severity of limb injury	{None, Mild, Moderate, Severe}	Fixed (Field Care)	Other
Upper Limb	Severity of upper limb injury	{None, Mild, Moderate, Severe}	Fixed (Field Care)	Other
Lower Limb	Severity of lower limb injury	{None, Mild, Moderate, Severe}	Fixed (Field Care)	Other
Head Injury	Severity of head injury	{None, Mild, Moderate, Severe}	Fixed (Field Care)	Other
Pen CW	Penetrating trauma in the chest	{No, Yes}	Fixed (Field Care)	Other
Brain Damage	Destruction or deterioration of brain cells	{No, Yes}	Fixed (Emergency Care)	Other
HT	Heamothorax	{No, Yes}	Fixed (Field Care)	Other
PT	Pneumothorax	{No, Yes}	Fixed (Field Care)	Other
Pen AW	Penetrating trauma in the abdomen	{No, Yes}	Fixed (Field Care)	Other
LB	Long bone fracture	{No, Yes}	Fixed (Field Care)	Other
UL amp	Upper limb amputation related to injury	{No, Yes}	Fixed (Field Care)	Other

Table C.1 – Continued

Variable Name	Variable Description	Variable States	Variable Dynamics	Variable Types
LL amp	Lower limb amputation related to injury	{0, 1, 2}	Fixed (Field Care)	Other
UP	Unstable pelvis	{No, Yes}	Fixed (Field Care)	Other
SF	Break in the cranial bone	{No, Yes}	Fixed (Field Care)	Other
GCS	Glasgow coma scale	Integer between [3,15]	Persistent	Other
Pupil Reaction	Pupillary response	{No, Yes}	Fixed (Emergency Care)	Other
Bleeding Limb BT	State of bleeding in the limb before treatment	{Mild, Moderate, Severe}	Persistent	Other
Bleeding Limb AT	State of bleeding in the limb after treatment	{Mild, Moderate, Severe}	Persistent	Other
Bleeding Pelvis BT	State of bleeding in the pelvis before treatment	{Mild, Moderate, Severe}	Persistent	Other
Bleeding Pelvis AT	State of bleeding in the pelvis after treatment	{Mild, Moderate, Severe}	Persistent	Other
Bleeding Chest	State of bleeding in the chest	{Mild, Moderate, Severe}	Fixed (Field Care)	Other
Bleeding Abdo	State of bleeding in the abdomen	{Mild, Moderate, Severe}	Fixed (Field Care)	Other

Table C.1 – Continued

Variable Name	Variable Description	Variable States	Variable Dynamics	Variable Types
Overall Bleeding BT	State of overall bleeding before treatment	{Mild, Moderate, Severe}	Persistent	Other
Overall Bleeding AT	State of overall bleeding after treatment	{Mild, Moderate, Severe}	Persistent	Other
RC BT	Deterioration in respiratory function before treatment	{No, Yes}	Persistent	Other
RC AT	Deterioration in respiratory function after treatment	{No, Yes}	Persistent	Other
O2 Sat	Oxygen saturation	{Normal, Abnormal}	Persistent	Other
RR	Respiratory rate	{Normal, Abnormal}	Persistent	Other
HR	Heart rate	Continuous	Persistent	Other
SBP	Systolic blood pressure	Continuous	Fixed (Field Care)	Other
Initial Threat	Threat before any treatment is applied	{Low, Moderate, Severe}	Fixed (Field Care)	Other
Overall Threat	Threat after treatment	{Low, Moderate, Severe}	Persistent	Other
Chest Decompression	Intervening to decompress the chest	{No, Yes}	Persistent	Treatment
Binder	Applying binder	{No, Yes}	Persistent	Treatment

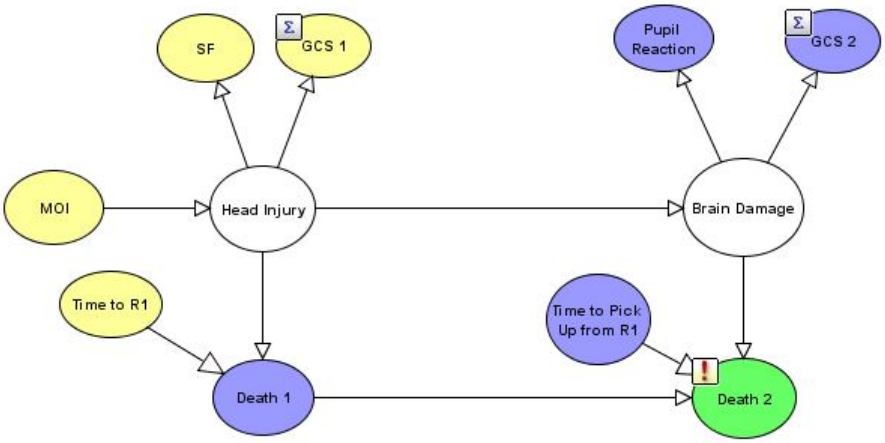
Table C.1 – Continued

Variable Name	**Variable Description**	**Variable States**	**Variable Dynamics**	**Variable Types**
Splintage	Applying splintage	{No, Yes}	Persistent	Treatment
Tourniquet	Applying tourniquet	{No, Yes}	Fixed (Field Care)	Treatment
Time to R1	Transfer time from point of wounding to the field care	$\{< 1$ hour, ≥ 1 hour$\}$	Fixed (Field Care)	Transition Time
Time to Pick Up	Time the soldier to be picked up from the field care by the emergency response team	$\{< 10$ min, ≥ 10 min$\}$	Fixed (Emergency Care)	Transition Time
Death	Event of death	{No, Yes}	Persistent	Target

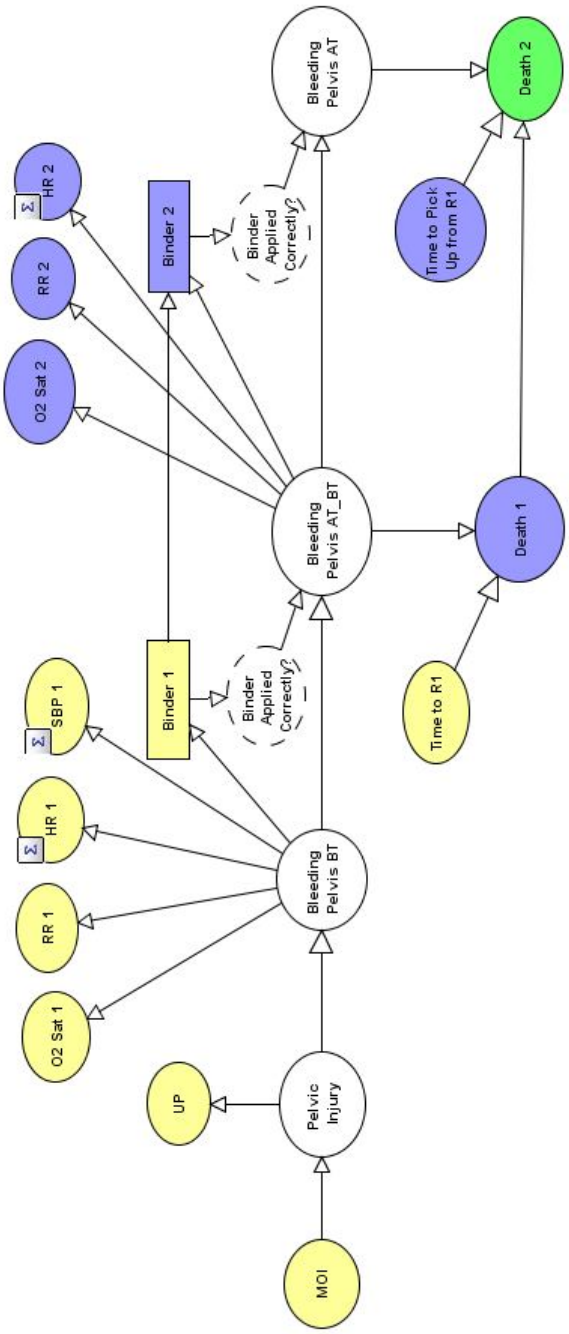
Appendix D

The sub-models related to the four triggers: head, pelvic, chest, and abdominal injury described in Chapter 5

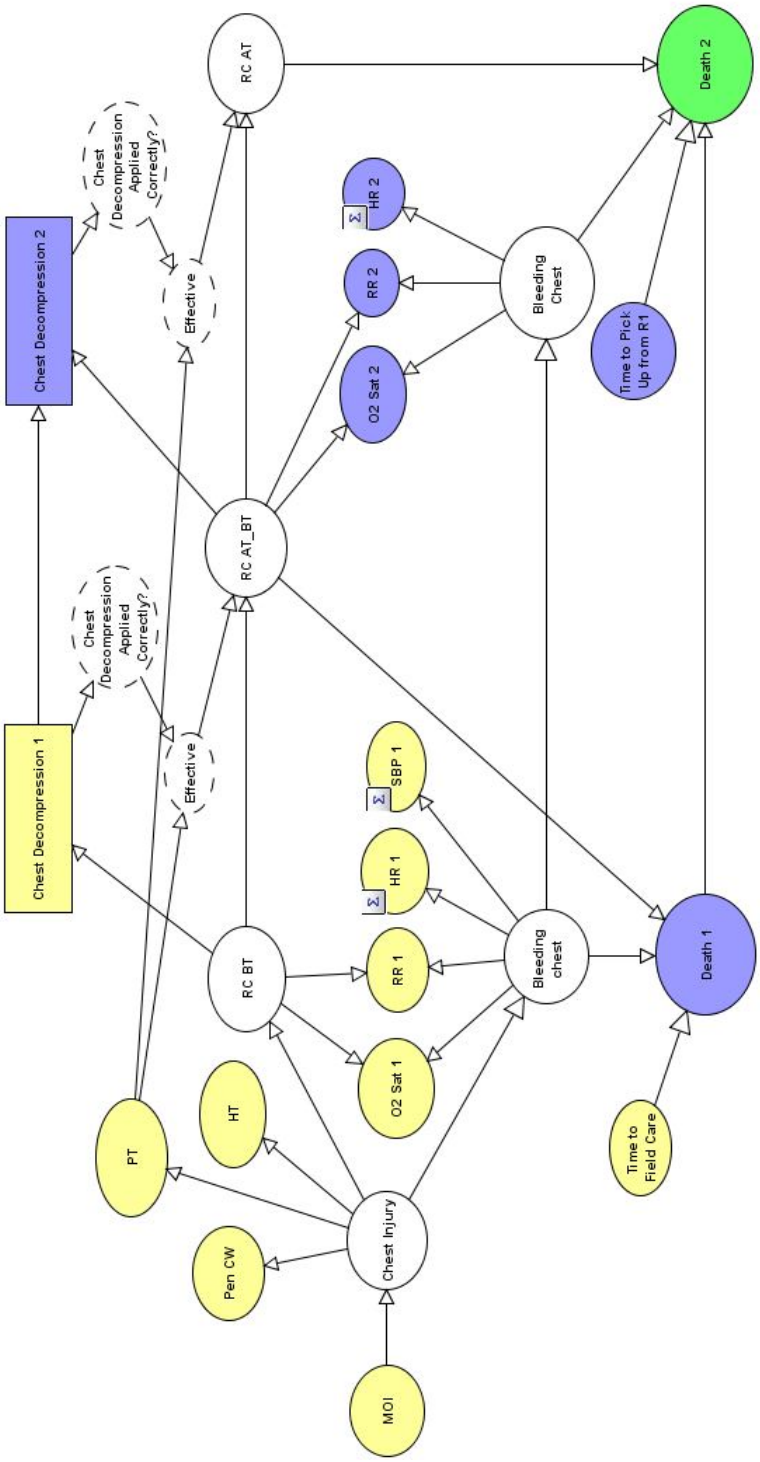
Head BN 1:2



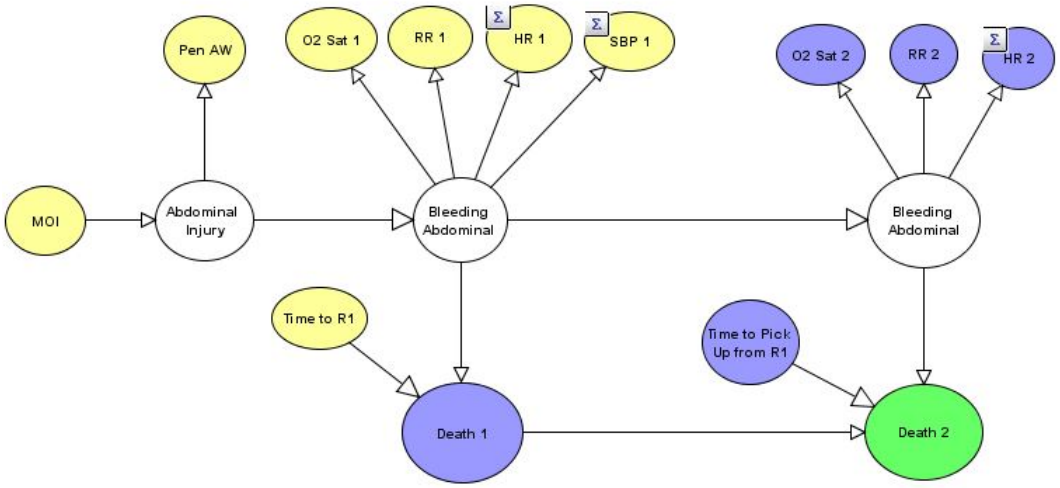
Pelvic BN 1:2


Bleeding Pelvis AT
Death 2
HR 2
Binder 2
Binder Applied Correctly?
Time to Pick Up from R1
RR 2
O2 Sat 2
Bleeding Pelvis AT_BT
Death 1
Binder 1
Binder Applied Correctly?
Time to R1
SBP 1
HR 1
Bleeding Pelvis BT
RR 1
O2 Sat 1
UP
Pelvic Injury
MOI

Chest BN 1:2


RC AT
Death 2
Chest Decompression Applied Correctly?
Chest Decompression 2
Effective
HR 2
RR 2
O2 Sat 2
Bleeding Chest
Time to Pick Up from R1
RC AT_BT
Chest Decompression Applied Correctly?
Chest Decompression 1
Effective
SBP 1
HR 1
RR 1
O2 Sat 1
RC BT
Bleeding chest
Death 1
HT
PT
Time to Field Care
Pen CW
Chest Injury
MOI

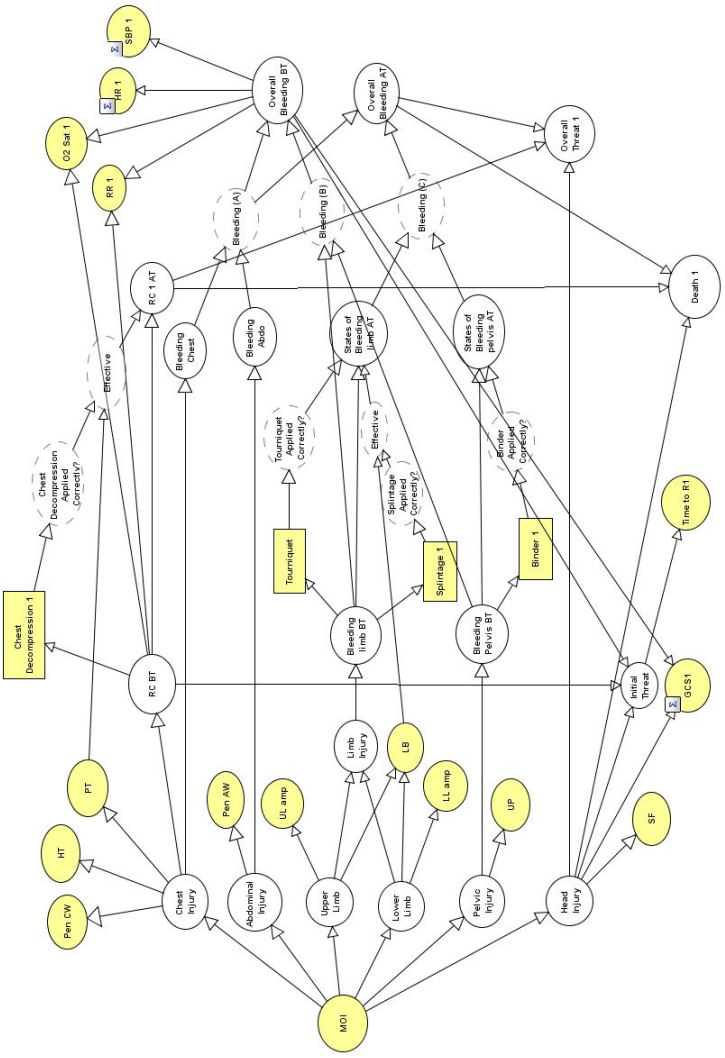
Abdominal BN 1:2



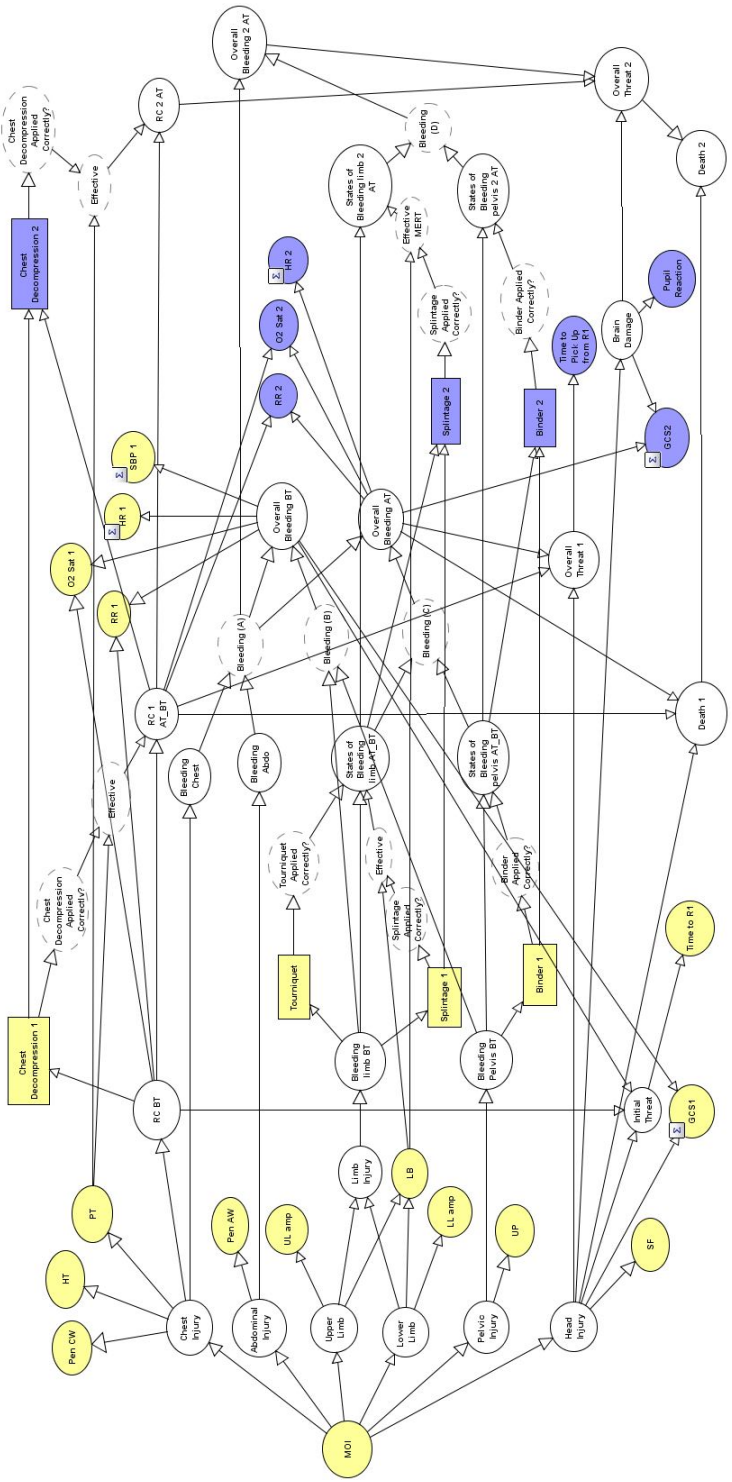
Appendix E

The complete BN in the two successive stages of care

Complete BN 1



Complete BN 1:2



Appendix F

Specifics of the 10 cases used in the evaluation study in Chapter 7

Cases	Pre-hospital	Emergency Room	True Outcome	Model's Prediction
Case 1	Age: 35	SBP = 130	Coagulopathic	17%
	MOI: Pedestrian vs Car	HR: 108		
	Energy: High	Chest X-Ray: Clear		
	HR: 110	LB: None		
	GCS: 8	Pelvis X-Ray: Overlapping bone of the pubic symphysis		
	Fluids: 1100mls	pH: 7.428, Lactate: 4, BE: -4		
Case 2	Age: 50	SBP = 68	Coagulopathic	47%
	MOI: Motorcycle vs lorry	HR: 130		
	Energy: High	Chest X-Ray: Multiple rib fractures		
	SBP: 137	LB: None		
	HR: 107	Pelvis X-Ray: Displaced pelvic fracture		
	GCS: 11	Fast: Positive		
	Fluids: 1250mls + 1g TXA	pH: 7.131, Lactate: 4.5, BE: -8.8		
Case 3	Age: 18	SBP = 121	Non-coagulopathic	0.7%
	MOI: Stab to abdomen	HR: 71		
	Energy: Low	GCS: 15		

Table F.1 – Continued

Cases	Pre-hospital	Emergency Room	True Outcome	Model's Prediction
	GCS: 15	LB: None		
	Fluids: None	Chest X-Ray: Free intra-abdominal gas		
		Fast: Positive		
		pH: 7.369, Lactate: 1.7, BE: 1..7		
Case 4	Age: 19	SBP = 136	Non-coagulopathic	6.5%
	MOI: Head on collision	HR: 125		
	Energy: High	Chest X-Ray: Haemopneumothorax, surgical emphysema		
	SBP: 138	LB: Yes		
	HR: 94	Pelvis X-Ray: No fracture		
	GCS: 14	Fast: Negative		
	Fluids: 250mls	pH: 7.353, Lactate: 2.0, BE: -1.3		
Case 5	Age: 51	SBP = 70	Coagulopathic	83.7%
	MOI: Cyclist vs car	HR: 120		
	Energy: High	Chest X-Ray: Haemopneumothorax, rib fractures		
	SBP: 91	LB: Yes		

Table F.1 – Continued

Cases	Pre-hospital	Emergency Room	True Outcome	Model's Prediction
	HR: 133	Pelvis X-Ray: No fracture		
	GCS: 4	Fast: Negative		
	Fluids: 250mls + 1 PRBC	pH: 7.019, BE: -14		
Case 6	Age: 26	SBP = 83	Coagulopathic	73.6%
	MOI: Male – one under	HR: 136		
	Energy: High	Chest X-Ray: Haemopneumothorax, rib fractures		
	SBP: 80	LB: None		
	HR: 160	Pelvis X-Ray: Unstable pelvis		
	GCS: 14	Fast: Positive		
	Fluids: 700mls + 2 PRBC	pH: 7.16, Lactate: 6.2, BE: -8.9		
Case 7	Age: 19	SBP = 165	Non-coagulopathic	4.35%
	MOI: Motorcycle vs car	HR: 106		
	Energy: High	Chest X-Ray: Clear		
	SBP: 118	LB: Yes		
	HR: 106	Pelvis X-Ray: No facture		
	GCS: 15	Fast: Negative		

Table F.1 – Continued

Cases	Pre-hospital	Emergency Room	True Outcome	Model's Prediction
	Fluids: None	pH: 7.362, Lactate: 1.1, BE: -0.5		
Case 8	Age: 85	SBP = 92	Coagulopathic	75.8%
	MOI: Pedestrian vs truck	HR: 127		
	Energy: High	Chest X-Ray: Clear		
	SBP: 74	Pelvis X-Ray: No facture		
	HR: 100	Fast: Negative		
	GCS: 15	pH: 7.13, Lactate: 7.4, BE: -11.4		
	Fluids: 500mls + 1 PRC			
Case 9	Age: 63	SBP = 102	Non-coagulopathic	17.8%
	MOI: Motorcycle vs car	HR: 123		
	Energy: High	Chest X-Ray: Surgical emphysema		
	SBP: 130	LB: None		
	HR: 110	Pelvis X-Ray: No facture		
	GCS: 8	pH: 7.551, Lactate: 4.4, BE: -9.9		
	Fluids: None			
Case 10	Age: 35	SBP = 168	Non-coagulopathic	11%
	MOI: Fall from height	HR: 120		

Table F.1 – Continued

Cases	Pre-hospital	Emergency Room	True Outcome	Model's Prediction
	Energy: High	Chest X-Ray: Pneumothorax, rib fractures		
	SBP: 130	LB: None		
	HR: 125	Pelvis X-Ray: No facture		
	GCS: 5	Fast: Negative		
	Fluids: 550mls	pH: 7.367, Lactate: 0.9, BE: -2.2		

Appendix G

Baseline questionnaire used in the evaluation study in Chapter 7

Pre hospital/Handover Information

1. What is your initial impression of this case in relation to Coagulopathy?

(__)---------(__)---------(__)---------(__)---------(__)---------(__)---------(__)

Not likely Somewhat likely Extremely likely

2. Why?
   Rank the available information from most important to least important.
   1. ----------
   2. ----------
   3. ----------
   4. ----------

3. What would you do next?

Resuscitation

1. What is your initial impression of this case in relation to Coagulopathy?

(__)---------(__)---------(__)---------(__)---------(__)---------(__)---------(__)

Not likely Somewhat likely Extremely likely

2. Why?
   Rank the available information from most important to least important.
   1. ----------
   2. ----------
   3. ----------
   4. ----------

3. What would you do next?

Appendix H

Follow-up questionnaire used in the evaluation study in Chapter 7

1. What is your impression of this case in relation to Coagulopathy?

(__)---------(__)---------(__)---------(__)---------(__)---------(__)---------(__)

Not likely Somewhat likely Extremely likely

2. Why?
   Rank the available information from most important to least important.
   (You can include the prediction of ATC)
   1. ----------
   2. ----------
   3. ----------
   4. ----------

3. What would you do next?

   ---

4. How much would you say that you trust the prediction of the ATC model?
   (Please indicate on the scale)

(__)---------(__)---------(__)---------(__)---------(__)---------(__)---------(__)

Not at all Somewhat Trust Trust Completely

5. How useful was the prediction of ATC for making an assessment?
   (Please indicate on the scale)

   i. It was useful for confirming my assessment:

(__)---------(__)---------(__)---------(__)---------(__)---------(__)---------(__)

Not at all Somewhat Useful Extremely Useful

   ii. It was useful for revising my assessment:

(__)---------(__)---------(__)---------(__)---------(__)---------(__)---------(__)

Not at all Somewhat Useful Extremely Useful

   iii. Other
   ---

6. If you were also given an explanation of the prediction of ATC, how clear was it? (Please indicate on the scale)

(__)---------(__)---------(__)---------(__)---------(__)---------(__)---------(__)

Very Confusing Confusing Clear Very Clear

Why? (Please justify briefly your answer to (6). Indicate what you liked or did not like.)
