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Bayesian Networks in Healthcare: *Distribution by Medical Condition*

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Highlights

- A review which identifies the medical conditions for which contemporary literature on Bayesian networks (BNs) have been focused.
- Finds that most attention has gone towards four primary health conditions.
- Identifies differences in the approaches used by authors between each of the four primary health conditions.
- Contributes to our understanding of how and what BNs are being considered for in healthcare.

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Abstract

Bayesian networks (BNs) have received increasing research attention that is not matched by adoption in practice and yet have potential to significantly benefit healthcare. Hitherto, research works have not investigated the types of medical conditions being modelled with BNs, nor whether there are any differences in how and why they are applied to different conditions. This research seeks to identify and quantify the range of medical conditions for which healthcare-related BN models have been proposed, and the differences in approach between the most common medical conditions to which they have been applied. We found that almost two-thirds of all healthcare BNs are focused on four conditions: cardiac, cancer, psychological and lung disorders. We believe there is a lack of understanding regarding how BNs work and what they are capable of, and that it is only with greater understanding and promotion that we may ever realise the full potential of BNs to effect positive change in daily healthcare practice.

Keywords: Bayesian networks, Healthcare, Medical conditions

1. Introduction

Bayesian Networks (BNs) have received increasing attention during the last two decades [1, 2] for their particular ability to be applied to challenging issues and aid those making decisions to reason about cause and outcome under conditions of uncertainty [3-5]. In 2016, the journal *Machine Learning* ran a special issue on *Machine Learning for Healthcare and Medicine* [6]. In explaining their motivation for that issue, the editors discussed how ever-increasing volumes of health data created potential for developing new knowledge that could improve the practice of patient care. Machine learning (ML) and artificial intelligence (AI) approaches have been proposed for a diverse range of health topics from genomics [7, 8] to treatment selection [9, 10] and outcome, prognosis, prediction [11]. A significant benefit of BNs over methods of pure ML from data is that BNs do not explicitly require massively large datasets. BNs can incorporate the accumulated knowledge of experts in circumstances where data are limited, and still produce meaningful and accurate decision-support systems. This paper is part of a larger effort to address the wide chasm between research enthusiasm for BNs and their lack of adoption in healthcare. The paper seeks to understand the medical conditions BNs are being used to model and make predictions for, and any apparent differences in their application between clinical domains, in order to shed light on how we may harness the potential of BNs in daily healthcare practice.

BNs are based on Bayes' theorem and use a graphical approach for *compact representation of multivariate probability distributions* and *efficient reasoning under uncertainty* [2]. Bayes' theorem is a formula for understanding how belief in the probability of phenomenon under observation evolves as knowledge of related influential phenomena increases [12, 13]. For instance, where multiple diseases present with similar symptoms making differential diagnosis challenging, clinicians must update their degree of belief about which illness is causing the patient's poor health as new information becomes available from diagnostic tests and physical examination of the patient.

There are three approaches for developing a BN; (1) using only data (data-driven BNs) (2) using only knowledge (expert-driven BNs), and (3) using a combination of both data and

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knowledge (hybrid BNs). Expert-driven and hybrid BNs, which supplement data with knowledge, could potentially be the most capable approach for supporting Learning Health Systems (LHS), precision medicine, and thus enabling personalised clinical decision-making from large collections of aggregated health data. LHS, which include such well-known types as clinical decision support systems (CDSS) [14], have experienced slow adoption and are not routinely observed in clinical practice [15-17]. This is particularly true for those LHS based on BNs [2]. While others have reviewed the scope for AI and ML in healthcare [18-20], in each case BNs have been overlooked.

Authors who have reviewed medical decision support models tend to provide a *brief but broad brushstrokes* view of either the ML or AI domain before focusing the bulk of their work on whichever method was their particular area of research interest. An example is [21] where the authors provide non-exhaustive lists and a brief glossary of domain-wide terms before focusing solely on learning approaches for neural networks, which are only one of a vast number of AI and ML types. In [18] the authors describe a list of ML algorithms but only expound on two from their research: support vector machines and neural networks. Attempts had been made to identify [19, 22] and even quantify [18] the broad scope of medical conditions and clinical questions or activities to which ML and AI respectively are being applied. However, *it was difficult from each author's method and descriptions to identify: (a) the search terms they had used; (b) a list of the medical conditions or clinical questions; or (c) an accurate accounting of the papers identified by and used in each study.*

The aim of this paper is to establish the medical conditions to which BNs are being applied as part of our wider effort [23] to determine the potential benefits and challenges being faced by those seeking to integrate BNs into daily practice. This paper seeks to achieve its aim by identifying and quantifying the range of medical conditions for which the healthcare-related BN models are being considered. This paper contributes to our overall understanding of the purposes for which BNs are being considered as a predictive or decision-making tool in the healthcare domain, and the differences in approach between the most popular medical conditions to which they have been applied. It is only through continued research to understand the challenges and issues that we may in future harness the potential of BNs to affect positive change, and improve patient outcomes.

This paper is organised as follows: Section 3 presents the method used to achieve the objectives of this paper as part of our larger scoping review. Section 4 presents the results, followed by a discussion of the general findings and their significance in Section 5. The paper concludes with a summary in Section 6.

2. Method

We used the literature collection from our scoping review on BNs in healthcare [23]. The search term used to derive that collection was:

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"(((Bayes OR Bayesian) AND network) OR (probabilistic AND graphical AND
                    model)) AND (medical OR clinical)"
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Terms such as "Bayesian networks" or "graphical probabilistic models" were used here because they are widely used in the targeted literature. Different ways for explaining the medical condition do occur: in some papers an exact condition is identified, while in others broader terms

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such as “medical or clinical application”, “medical or clinical condition”, or “medical or clinical setting” are used. Our scope review settled on the broader terms “medical” and “clinical” as they were found in a wider collection of papers. There are many thousands of possible medical conditions that might be targeted by some form of *clinical decision support*, *artificial intelligence* or *machine learning* system. It would be impossible to perform separate searches for each medical condition and each variation of clinical terminology, and such a search would impose an unintended restriction on the papers returned by excluding the opportunity for a natural and broadly representative sample. The terms chosen also allowed papers to be returned from clinical and non-clinical sources describing solutions that may be in clinical use, or which may have been used in a clinical trial. This was important for assessing *adoption*, which is the topic of a future paper in our series on *BNs in Healthcare*.

Our initial and unrestricted search returned almost 100,000 papers which we contend was an impossible number to review, and therefore required some focus that we established not to affect the aim of this paper, nor reduce the efficacy of the search outcome. While using the same keywords, we limited the keyword search to identifying instances only in the title and abstract, reducing the initial number of papers returned to 3810. Through the process described in Figure 1 we then excluded papers published before 2012, as the aim of this paper is to review papers providing the state-of-the-art, rather than to provide a complete archaeology of BNs in healthcare. We also removed those not published in English, and any whose primary content was not healthcare-related. In addition, papers that did not provide BNs and instead were focused merely on Bayesian statistics or meta-analyses were excluded. Graphical models, such as *naive BNs*, which are the simplest BNs and structurally assume all variables are independent, and other graphical computational approaches used in ML or AI, including *neural networks*, have also been excluded. This review focused on published works, which means commercial products not associated with published academic or research papers may not have been included. Generally, works that fall outside the identified body of existing literature are naturally excluded from a review. As a rule, this limitation is inherent in the majority of published academic literature reviews.

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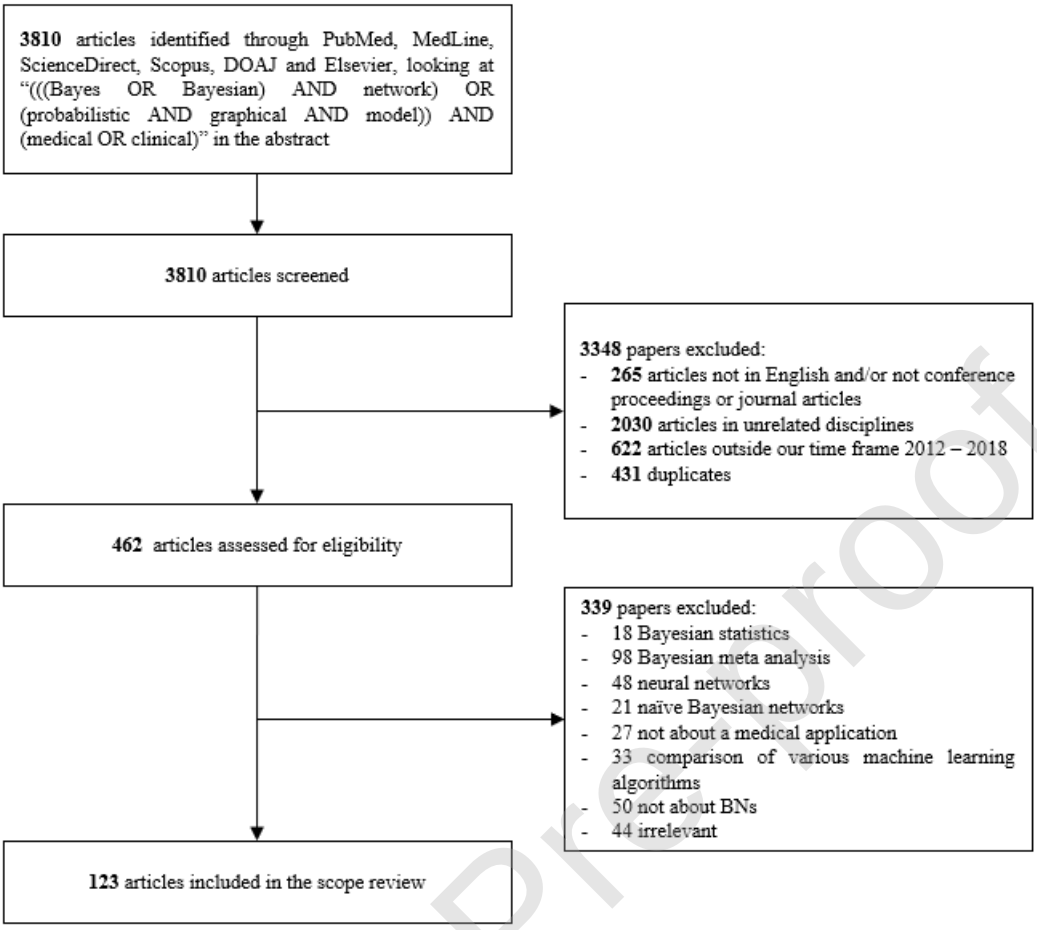

Figure 1: PRISMA diagram (from [23])

Our initial review plan from [23] identified six primary objectives that would be investigated during review of the literature collection. Given the interrelationship between components of Objectives 1-3, they are reported together in our main review in [23]. Standalone Objectives 4 and 6 will be the topic of works yet to be presented. Objective 5, also a standalone topic, is the focus of research presented in this paper which reports the distribution and frequency of medical conditions that have been the target for BN models in the same literature collection. Objective 5 is identified in purple in our review concept plan [23] presented here as Figure 2.

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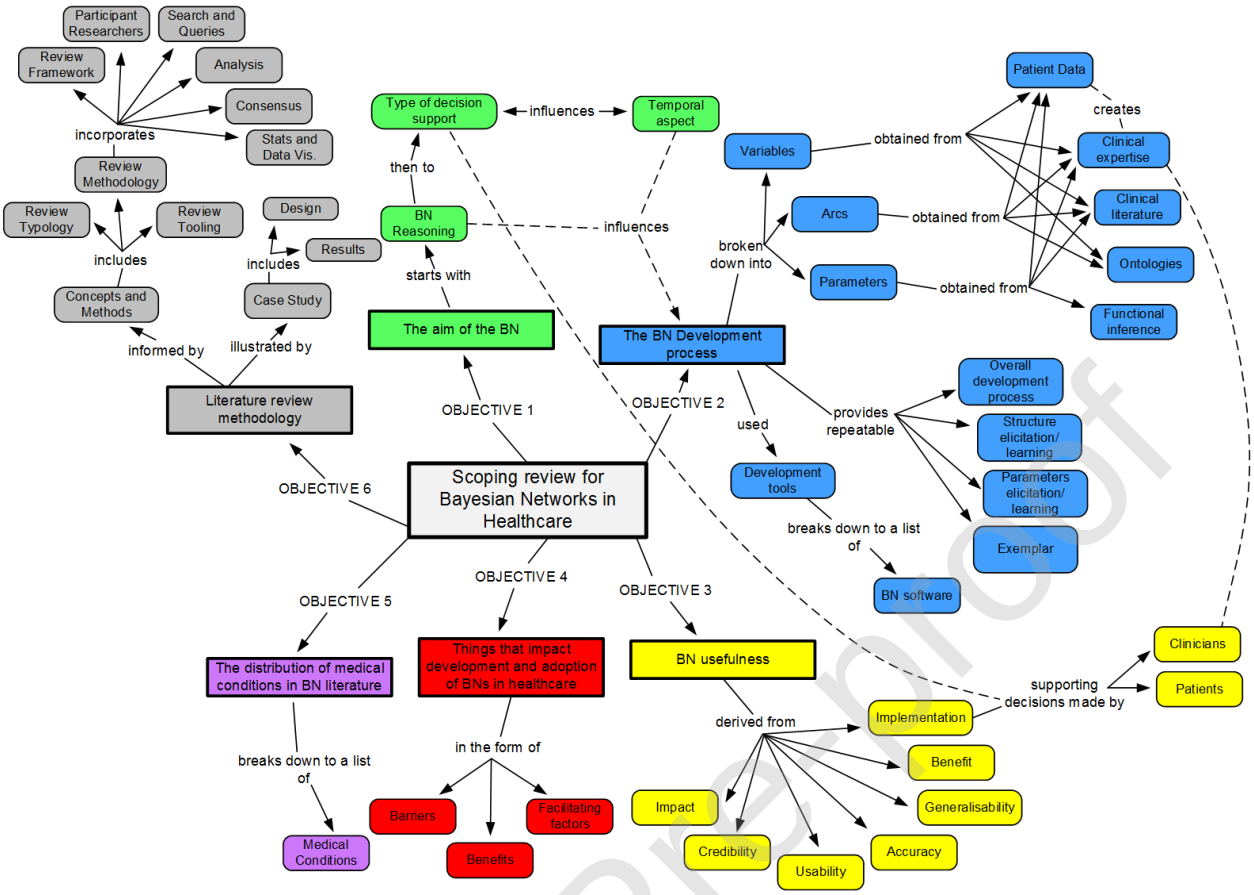

Figure 2: Concept map for the Scoping Review of Bayesian Networks in Healthcare (from [23])

The list of medical conditions in Table 1 was developed with the input of two clinical experts and refined inductively during a small-scale preliminary review described in [2]. Each paper was reviewed by two reviewers who recorded the target medical condition against the list which was presented to reviewers as part of a secure online survey used to manage and conduct the overall review. Where the medical condition was not listed, or the reviewer felt unable to make an explicit classification, it was possible to manually enter details or references to the condition from the literature into a free-text field exposed below the list. Where the two responses for a given paper differed, two authors (SM and EK) reviewed the paper collaboratively to achieve consensus. In rare circumstances where consensus could not be achieved, a clinician was available to assist with classification.

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	Medical Condition	Exemplar Citations
1	Blood disorders	[61, 63]
2	Brain or spine (including CNS injury)	[64]
3	Chronic Conditions (e.g.: diabetes and arthritic conditions)	[65, 66]
4	Cancer	[30-32]
5	Cardiac conditions	[25-27]
6	Fatigue	[67]
7	Genetic	[68]
8	Infectious diseases	[69]
9	Liver disease	[70, 71]
10	Lung and breathing disorders	[46-48]
11	Medication (concentration or reaction to)	[72]
12	Musculoskeletal Conditions	[73]
13	Oesophageal disorders (swallowing or speech)	[74]
14	Organ disorders or failure	[75]
15	Pregnancy disorders	[76]
16	Psychological or psychiatric disorders	[41-43]
17	Skin (burns or disorders)	[77, 78]
18	Sleep disorders	[79]
19	Surgery related infection	[80]
20	Utility of or experience of healthcare	[81]
21	Unclassified or Other	[52, 82]

Table 1: list of Medical Conditions

3. Results and Discussion

Even though the quantity of BN literature is rapidly increasing, it was possible to identify a distinct focus on a small group of conditions. Specifically, as shown in Figure 3, cardiac conditions, cancer, psychological and psychiatric disorders, and lung and breathing disorders made up 59% of the medical conditions in the literature. This result was not surprising given that other research identified similar disease foci for AI generally [18], and the notoriety of these conditions in the mainstream media as those *most likely to kill you* [24]. The remaining 41% of papers were spread across a diverse collection of seemingly random topics. Figure 3 also illustrates the general distribution of BN literature against the entire list of medical conditions. The complete review

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dataset is available as a supplemental material spreadsheet on the PamBayesian website at (http://www.pambayesian.org/interim-data/).

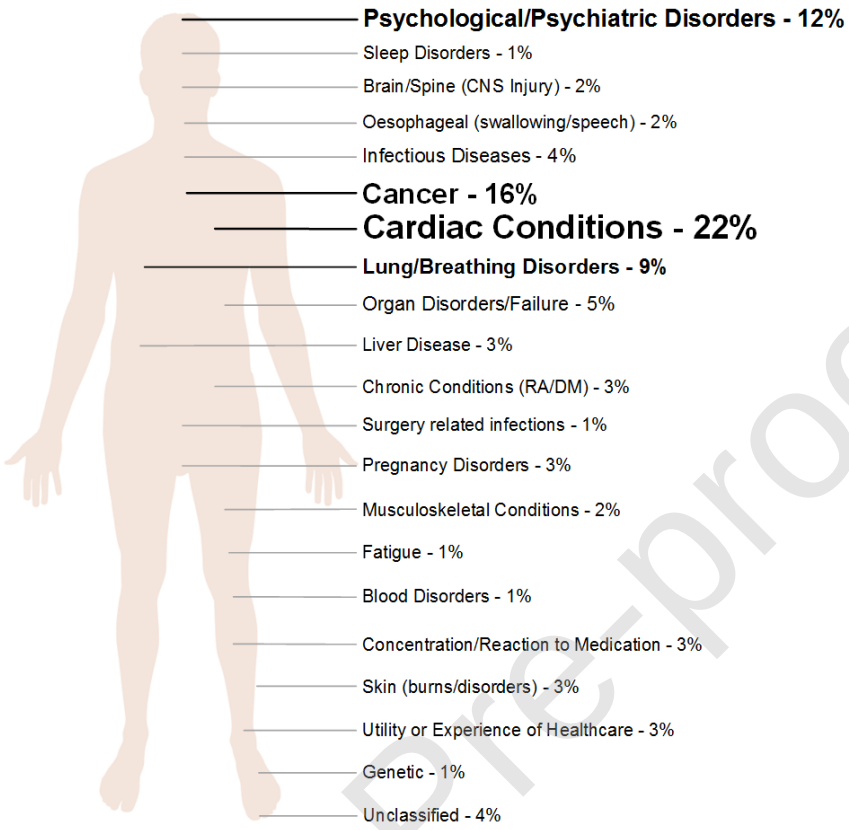

Figure 3: Distribution of medical conditions in BN literature

3.1 Most Common Medical Conditions

While in the dataset we have made available as supplementary material to the paper we identify every paper and distinct sub-classification for each, in this section we briefly examine only the most common or frequent topics discussed for each of the most common medical conditions.

Cardiac conditions

A strong theme for cardiac models was a restriction of focus to either *acute diagnosis* or *prediction of disease progression*. Common to many was the authors' use of electronic patient data as the primary source for elements of BN structure and observations necessary for prediction. This, while simultaneously admonishing the poor quality they observed of most available electronic health record (EHR) data and the limitations that arose from this quality issue [25-27]. Proposed approaches ranged from models for classifying the diagnosis [28] or severity [29] of a patient's condition, to prediction of risk for acute clinical events [25] and the likely progression of the individual's disease [26]. It was not unusual for cardiac BNs to incorporate known comorbidities and validate their interaction with the patient's cardiac condition [26, 27].

Cancer

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Breast cancer [30-32] and (onco)gene expression [33] separately, and sometimes together [34, 35], were the targets receiving the greatest attention for the topic of cancer. BNs were applied to supporting and enhancing expert knowledge in diagnosing breast cancer from mammography images [36], classifying tumours [30], and as a potential method to improve expert judgement in situations where increasingly complex treatment options have made clinical decisions difficult [37]. Cancer BNs were more likely to seek previously unknown relationships either between symptoms and syndromes [38], or expressed genes and target metastatic cancers [34].

Psychological and psychiatric disorders

The most prevalent conditions modelled in the literature were depression [39-41] and the age-related cognitive degeneration diagnoses: dementia and Alzheimer's Disease (AD) [41-43]. Incorporating an organisational structure from ontologies and merging this with BNs was a popular approach in these medical models [39, 44], along with a stronger focus on identifying or relying on a hierarchy of symptoms [39, 44]. While medical models were generally seen to be more likely to draw on experts' knowledge than data alone, the nature and mystery of psychological and psychiatric disorders may be the reason they more frequently drew on clinical expertise during BN development [39-41, 43, 45].

Lung and breathing disorders

Half of all models for lung and breathing disorders sought to predict the risk of exacerbation of an already diagnosed chronic clinical condition, including: chronic obstructive pulmonary disease (COPD) [46, 47] and asthma [48]. Others sought to use clinical signs and symptoms to either assess the probability of a particular acute pulmonary diagnosis [49], predict future severity [50], or classify the subtype of the diagnosed disease [51]. One approach proposed a mobile smartphone app that used questionnaires and a BN model to ascertain the patient's current condition and provide contextually relevant advice, while delivering data on the patient's health status to clinicians via an internet connection and a central server [46]. This is similar to the approach proposed by the authors of this paper for their PamBayesian project (www.pambayesian.org).

3.2 Researcher and Content Classification

Overall, papers could generally be classified as one of three types. *First,* there were papers written entirely by computer scientists and mathematicians that whilst being dense on technical detail and description for the math of BNs, were sparse on clinical detail for the conditions being modelled - these we describe as *method-driven* [28, 39, 52, 53]. *Second,* there were those that were written entirely by clinicians who included comprehensive discussion and contextualisation of the medical condition and its symptomatology, but significantly less technical discussion of the theory and development of their BN - these we felt were *problem-driven* [54, 55]. *Finally*, there were those presented by a mix of both clinicians and computing or decision scientists - these we describe as *hybrid-driven*.

In *method-driven* works, the focus is mainly on the BN methodology. A medical application is used simply as a case study to evaluate the proposed methodology.

For *problem-driven* works, it was rare to find a paper that whilst appearing to be written entirely by clinicians, was methodological in both its regard for the BN's development process and

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comprehensive in its technical description of the BN generally. One such unicorn paper drew the attention and comments of both reviewers [56]. The reviewers also generally felt that radiologists came across better than most other clinical disciplines at describing the mathematical and technical aspects of BN development, possibly resulting from their medical physics training [57, 58].

In *hybrid-driven* works, authors tended to introduce both the medical condition (the problem aspects) and BN theory (the methodology aspects) early [48, 59-62]. Having a multidisciplinary team offered the advantage that both aspects generally received equal space and descriptive detail in the paper. From the medical perspective, the research problem and benefit of the BN to clinical practice are better explained. From the computing point of view, the overall BN development process is described in greater detail. In papers where both clinicians and computer scientists are involved the BN development and validation process were found to possess greater accuracy, as clinical input was considered.

3.3 Strengths and Limitations

A strength of this review is that this is a component of the largest scoping review of BNs in healthcare [23]. Another strength is that tools, including a structured list of medical conditions and an online standardised survey form were developed to ensure a consistent review process.

A limitation of this review is that, even if this is a representative sample of papers published in both medical and AI journals and conference proceedings, it may not reflect the entire range of the literature regarding BNs in healthcare. We looked for keywords such as “Bayesian Networks”, “probabilistic graphical models”, “medical”, “clinical” to appear in the abstract of each paper. While it would not constitute a significant number, it is possible that some relevant papers were not included because they did not use the selected keywords in their abstract. This is especially true in cases where the actual name of the medical condition is described without mentioning the words “medical” or “clinical”. However, we believe that the large number of selected papers was sufficient for drawing conclusions.

Because of the very large number of published papers and the time needed for review and data extraction, we limited the study to the seven-year period 2012-2018. However, we acknowledge this has left out early implementations of BNs that included for instance HUGIN [83] and Pathfinder [84]. We also note that the most recent patents for Pathfinder [85, 86] make no mention of the use of Bayesian networks in the current Pathfinder software, which may suggest the authors have the BN approach in their most recent releases of the software tool. We believe this is a safe number of years to be able to draw conclusions for the purpose of this paper. As the review began in early 2019, we chose not to include papers published in those first few months of 2019. We do not believe this exclusion had any significant impact on our findings.

It is possible that evidence of commercially available applications using BNs may not necessarily be in journal articles, appearing in other places, such as company reports, media (grey literature) and general commentaries. For example, based on limited marketing materials there are indications that Babylon have used BNs in their non-public research and application development [87], including what is claimed as potentially the largest BN in the world [88]. As a result, BNs like these may not be represented in this review. This is a limitation inherent in all literature reviews.

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4. Summary and Conclusions

This paper began by recognising that while other authors had reviewed, and in some cases identified and quantified the medical conditions for which other AI and ML methods had been developed, in all cases they had eschewed BNs. This was our primary research problem. We also highlighted three secondary issues present in those reviews. That it was often difficult to identify: (a) the search terms they had used; (b) a framework or description for medical conditions; or (c) an accurate accounting of the papers identified by and used in each study.

As a core component of our systematic review of BNs in healthcare, our reviewers worked with clinicians to develop a list for use in identifying the target medical conditions that had been the focus of BN modelling. To address the primary research problem, we quantified the BNs from our literature collection by medical condition, identifying four conditions that received the majority of attention from authors and reviewing papers from each of those conditions in greater detail. Also, to ensure we did not proliferate the three secondary issues observed of other works, we provided: (a) the search term and process used to arrive at our literature collection; (b) the list of medical conditions that reviewers were asked to use in classifying medical BNs; and (c) a URL link to the complete review dataset.

BNs have and continue to receive significant interest for their ability to combine available evidence and accurately reason under conditions of uncertainty. This paper has contributed to our understanding of how and what BNs have been considered for in healthcare. We identified the four primary conditions that have received almost two-thirds of BN-modelling attention in the literature: cardiac, cancer, psychological and lung disorders. We also found a number of acute differences in how BNs were being applied to each.

The wider observation is that despite the strong research interest in BN models in healthcare, this interest is not matched by adoption in practice. It is possible that with most BN in healthcare research effort going to these four primary conditions that already receive vast amounts of funding and attention from other solution areas, that BNs are being drowned out: effectively lost in the noise. It is also possible that a lack of understanding pervades with respect to how BNs work and what they are capable of. Either way, it is only through understanding and promotion, continued multidisciplinary research and adherence to the full disclosure required of the scientific method that we may in future harness the potential of BNs in daily healthcare practice and affect positive change, improving outcomes for clinicians and patients alike.

Conflict of Interest

AUTHOR DECLARATION TEMPLATE

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing

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of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

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