

Bayesian Network Models of Causal Interventions
in Healthcare Decision Making:
Literature Review and Software Evaluation

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Contents

Introduction	3
Literature Search Strategy and Analysis	3
Review of Relevant Articles	5
Interventions and Diseases Management: Risk Boundary Selection	8
Review Summary and Model Selection	9
Experimental Evaluation	9
References	19
Appendix A	20
Appendix B	32
Appendix C	44
Appendix D	49

Abstract

This report¹ summarises the outcomes of a systematic literature search to identify Bayesian network models used to support decision making in healthcare. After describing the search methodology, the selected research papers are briefly reviewed, with the view to identify publicly available models and datasets that are well suited to analysis using the causal interventional analysis software tool developed in [1]. Finally, an experimental evaluation of applying the software on a selection of models is carried out and preliminary results are reported.

Introduction

In the medical field, prediction of the risk of disease requires establishing a statistical model of risk factors and diseases, and prediction of the probability of disease according to levels of multiple risk factors. Bayesian network models are often used in healthcare settings to support decision making, such as outcome prediction and disease management. Since Bayesian network models can support causal inference and interventions, algorithms and software tools have been developed, for example [1], that can compute provable robustness guarantees and automate “what if” analysis of disease outcomes. However, in view of data often being proprietary and privacy concerns, there is a lack of publicly available models and datasets on which to evaluate the potential of these methods in healthcare settings.

This report summarises a systematic review of existing literature on Bayesian network models in medical settings undertaken as part of the FUN2MODEL project², with a specific focus on decision support that is based on causal interventions. A search methodology was developed to identify articles that meet a set of criteria, which were then reviewed to summarise the use cases, including the medical domain and effects of causal interventions, and insight obtained; those articles that provide publicly available models and datasets were highlighted. For a selection of models, causal Bayesian network representations were built and analysed using the IntRob software [1]³, and preliminary results reported.

Literature Search Strategy and Analysis

This review is focused on identifying existing datasets and Bayesian network (BN) models that capture decision making in healthcare settings, and particularly those where the decision can be modelled as a causal intervention in the system. Thus, articles were selected based on the following criteria:

- availability of the (Bayesian network) model;
- availability of (categorical) data;
- appropriate targets for intervention (for example, administering a drug);
- clear intervention interpretation to determine the appropriate intervention bounds;
- an appropriate target probability (e.g. survival of patient).

A comprehensive search of health and health informatics literature databases, including PubMed, ScienceDirect and Scopus, was performed using keywords arranged in the following general search query:

bayes AND (network OR model) AND (medical OR clinical) AND decision-making AND causal

Terms such as ‘Bayesian networks’ and ‘decision making’ are included as they are widely used in the target literature. We also tried using ‘intervention’, but this proved to be less useful as intervention is also a medical term. In particular, in medicine, an intervention is a treatment, procedure, or other action taken to prevent or treat disease, or improve health in other ways [2]. As for interventions in BNs, in Woodward’s theory [3] one variable X is a direct cause of another variable Y if there exists an intervention on X such that, if all other variables are held fixed at some value, X and Y are associated. Such an account assumes a lot about the sort of intervention needed, however, and Woodward goes to great lengths to make the idea clear [4]. A preliminary search showed that there is a small amount of work in this specific area, so the term ‘causal’ was chosen as the most universal one, encompassing also the interventions that we are interested in. Due to the large number of articles, we limited the selection to the areas of Computer Science, Psychology, Medicine and Dentistry, and Neuroscience, using filters.

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²fun2model.org

³<https://github.com/wangben88/interventional-robustness>

After extracting relevant articles based on the above criteria, we analyzed each article using natural language processing (NLP) tools to answer the following questions: in what medical areas are Bayesian network models used, and, in particular, what were the effects of causal interventions studied? For each article, we had access to the following attributes: title, abstract, authors, year, and DOI. The analysis was performed on the basis of available abstracts of articles. As of August 4, 2022, there were 1042 (983 in ScienceDirect; 24 in Scopus; 35 in PubMed) unique article abstracts available to download in ScienceDirect, Scopus and PubMed.

The entire procedure/algorithm for the analysis of the articles is shown in Appendix A in Figure A.1. In the first step, the PMIDs of the PubMed articles were converted to the BibTeX format. Then, DOI links from all three databases were converted into the same format and merged, allowing us to remove duplicate articles from the database. For the remaining articles, we extracted the article abstracts; 29 abstracts were not available.

Next, all raw abstracts were cleaned/preprocessed in order to facilitate further analysis. We used regular expressions (combinations of wildcard characters operators for searching and manipulating substrings in text) to remove all parentheses in abstracts, and tokenize the words. Tokenization allows us to decompose the text into a sequence of tokens, which can be words or sub-words.

We then removed all stop words. Stop words in natural language are the most common words which do not convey significant meaning; for example, in English these are words such as ‘the’, ‘for’, ‘at’, ‘to’, etc. English and French dictionaries were used to identify and remove the stop words. We also perform lemmatization of the tokens, which refers to converting a token to its ‘base’ or ‘dictionary’ form. This process includes, for instance, plural to singular conversion, as well as word tense normalization. Unlike stemming (another popular approach which simply removes affixes), lemmatization takes into account a broader context, including the surrounding and adjacent clauses. Finally, we employ N-grams, which are continuous sequences of tokens in a document. Bigrams (2) and trigrams (3) were used in our analysis.

For the final step, Latent Dirichlet Allocation (LDA) was used as a statistical model for the abstracts. LDA models every document as a mixture of topics, and every topic as a mixture of words. Crucially, it is possible to simultaneously estimate both parameters: finding a combination of words associated with each topic, as well as determining a combination of topics that describe each document (in this case abstracts). The LDA model was built with 30 different topics, where each topic is a combination of keywords and each keyword contributes a certain weight to the topic. After training, we obtained the following evaluation for the LDA model:

Perplexity: -15.231877825584922
Coherence Score: 0.4339549814094681

Perplexity measures how well a probability distribution predicts a sample; it thus indicates how well the topic model fits the data. Coherence, on the other hand, measures the degree of semantic similarity between words in a topic, in order to measure how ‘meaningful’ each topic is. The lower the perplexity, the better the model, and vice versa for coherence. While perplexity is an important measure of fit, we are more interested here in obtaining a conceptually coherent/consistent topic model. Therefore, in this analysis, we primarily consider the coherence score.

According to non-optimised LDA analysis, a vast proportion of the retrieved articles are in the field of research on cancer and mental disorders. This is indicated by word markers such as ‘death’, ‘cognitive’, ‘brain’, ‘emotion’ and ‘behaviour’ (see Appendix A A4-A8). On the charts, circles represent the topics. The larger the circle, the more common this theme. A good topic model should have large non-overlapping circles scattered throughout the diagram. In turn, a model with too many topics will often have many small circles that can overlap and be in the same area of the chart.

To optimize the model, hyperparameter tuning was performed. For this, the coherence score was calculated for 10 topics, for a range of values of alpha and beta hyperparameters. The maximal coherence score was obtained using 10 topics, alpha = 0.01, and beta=0.91. After the selection of hyperparameters, the accuracy of the model was:

Perplexity: -8.210963741472142
Coherence Score: 0.643855950055103

The model has become more coherent, but less sensitive. In Figure A7 in Appendix A, we see that the top-30 most salient items include tokens such as ‘brain’, ‘cognitive’, ‘death’, ‘neural’, ‘intervention’, ‘memory’ and ‘child’. According to the model, a possible interpretation is that the interventions are probabilistically relevant to 37.5% of the topics in which the study was conducted. In the distance map, the first bubble includes generic terms that can be found in almost all medical works. The behaviour token is relevant to three large clusters; it can be ignored. The second large cluster includes tokens such as ‘intervention’, ‘death’, ‘treatment’, and ‘child’. This may be due to the fact that research on interventions is mainly conducted on fatal diseases that children suffer from. The third large cluster of tokens relates to diseases associated with a decline of brain function. This can be observed if the relevance metric (λ) is 0.6. The fourth and fifth clusters are language

clusters, such as Spanish and French. Other clusters represent a small percentage of the total and are mostly devoid of particular semantics.

In Appendix A, Figure A2 shows the search results for all three databases. From ScienceDirect, in the Computer Science field 257 papers were downloaded (out of 258), in the Medicine and Dentistry fields 609 papers were downloaded (out of 632), in the Neuroscience field 342 papers were downloaded (out of 382), and in the Psychology field 271 papers were downloaded (out of 305). In total 1479 papers were downloaded and after duplicate removal 1093 papers were retained. Our overall finding is that the bulk of the analyzed work is in the areas of cancer, respiratory diseases and brain research. Interventions are likely to be found in studies that investigate disease deaths (e.g., cancer and COVID-19). A search was carried out for relevant data in the articles. Due to missing data, only 34 articles were included in this report.

Review of Relevant Articles

Due to variability in presentation of diseases, it can be difficult for doctors to prescribe optimal treatment plans. More accurate predictive models can be beneficial to provide personalised treatment and determine effective interventions. At the same time, it is important that any interventions we apply are safe; a medical error in any specific intervention could be fatal. This may be due to the individual reactions of the patient's body to drugs or on the part of the doctor, for example, loss of concentration. From a practical perspective, rigorously testing all potential interventions/treatments for all types of patients in long clinical trials is not always feasible as valuable time may be lost, and the result may not be positive. As a result, doctors often have to rely only on their experience, and the wrong choice of intervention may aggravate the course of the disease. In this review, we are interested in applications of causal inference to help solve the 'treatment effect' problem. In this context, one aims to choose an intervention which has a positive causal effect on the outcome variable, which will help to determine the most effective treatment plan. The effect of an intervention can be formalized as the difference between two potential outcomes for an individual: one where they receive the intervention, and one where they do not. As a result, counterfactuals are the basis for causal conclusions, giving answers to a number of questions [5]. For example:

1. will the intervention work?
2. why did it work?
3. what combination of interventions are safe/can reduce the risks?
4. how effective is the intervention?

Unfortunately, in many articles, the concept of intervention is extremely vague. In particular, as mentioned previously, in medical articles interventions are usually understood as operational actions rather than part of a model. Also, in more than 90% of cases, data or models are not available. Thus, we selected all papers with medical data available for review. A brief summary of the relevant articles now follows.

Several papers demonstrate applications of Bayesian network analysis in cancer research.

In [6], the authors build a Bayesian network model using the English Lung Cancer Database (LUCADA) and apply causal interventions. The results show that the survival-maximizing model only works correctly in 29% of cases. This is due to the lack of some of the information necessary for effective interventions; in the database, the constructed model is not able to distinguish between patients for whom surgery is indicated and those for whom it is not suitable. The model and data are not available. The authors continue their work in [7], where a clinical decision support application for lung cancer care (LCA) was developed. The goal was to help lung cancer experts make decisions about treatment choices in MDT (Multidisciplinary Team) meetings. The system is not available via the link in the article (the login page is stored in the webarchive).

The impact of obesity in early-stage breast cancer survivors on health behaviors was studied in [8]. Clinical data from 333 overweight or obese postmenopausal women who survived breast cancer were used to build a Bayesian network. The authors combine factors to determine possible interventions. For example, based on the network they developed, they conclude that older age, more sleep disturbances, and higher BMI are associated with lower physical activity. Data is available in the article, but presumably, after the anonymization of the personal data, some parameters were removed. Because of this, the dataset is incomplete. It may be possible to synthesize the missing data based on what is already known.

Factors and causal relationships influencing the choice of place of death in Swiss cancer patients were studied in [9]. One of the goals of the project was to explore the possibility of interventions provided by healthcare professionals to facilitate EOL (end of life) at home. The model was built on 116 adult patients who died from cancer between 2015 and 2016 in southern Switzerland. The model can be downloaded from the supplementary materials. Data is available on request.

Using data from the National Lung Screening Trial (NLST), a model is built in [10] to study the impact of interventions on the survival of patients with lung cancer. By interventions, the authors mean low-dose computed tomography (LDCT) irradiation to reduce patient mortality. The authors constructed their dynamic Bayesian network (DBN) using 10-fold cross-validation. The models were evaluated based on the probabilistic variable of the biopsy, taking into account all previous and current data for each of the three intervention points in the NLST study. Data is available upon request.

For the diagnosis of breast cancer, researchers used a Bayesian network [11] built using the K2 algorithm. The data is collected from The First Affiliated Hospital of Fujian Medical University, China and the Breast Cancer Wisconsin Dataset (BCWD) of the UCI machine learning repository. Naive Bayes (NB), Bayesian network (BN), ID3, J48 and NBTree classifiers are used for performance analysis. The UCI dataset is available for download.

In [12], the authors (using transcriptomic datasets) build a DBN model used for cancer classification. They used three datasets for a DBN-based approach, which is able to model time series gene expression data for classification purposes. The datasets are the pancreatic cancer dataset (GSE14426), colon cancer dataset (GSE37182), and breast cancer dataset (GSE5462). Data is available through GEOquery package.

Analyzing multiple primary cancers is a challenge. In the study of [13], the authors build a BN model to describe the occurrence of two primary cancers to predict five-year patient survival. They compare the performance of models with BPNN, Logistic Regression (LR), Support Vector Machine (SVM) and Naive Bayes (NB). Resulting conditional probabilities and the model are available in the paper.

Preoperative identification of patients at risk for lymph node metastasis (LNM) is challenging in endometrial cancer [14]. The authors develop a BN model to predict LNM and outcome in endometrial cancer patients. They constructed the dataset from a retrospective multicenter development cohort from 10 centers across Europe. The model predicts 1, 3 and 5-year survival and was tested on 2 external cohorts from the Netherlands and from Norway. The trained model is available.

Breast cancer is the most common cancer in women. Clinicians face difficult decisions in many aspects of breast cancer treatment. In [15], the authors developed a Bayesian network called Causal Modeling with Internal Layers (CAMIL) for preventing breast cancer metastasis. A decision support system (DSS) based on this model, called DPAC, was developed and tested by 5-fold cross-validation. The system can recommend related treatments for patients based on not only mutation profile but also their histopathology and clinical parameters. A dataset called LSDS-5YDM is available.

Due to the emergence of COVID-19 disease, there is a need for Contact Tracing Apps (CTA). But there have been concerns about the privacy of such applications. In [16], the authors propose a model based on the user's decisions about the confidential data provided to them. Based on the data, the model predicts the likelihood of the presence of asymptomatic, mild or severe COVID-19. The authors performed a sensitivity analysis for the 'eventual COVID19 status' node. It shows which yet unobserved factors have the greatest impact on the target node. The full BN model is available.

In [17], researchers studied what model is best for classifying COVID-19 given overall symptoms. They conducted experiments with Logistic Regression (LR), Support Vector Machine (SVM), Naive Bayes (NB), Decision Tree (DT), Multilayer Perceptron (MLP), Fuzzy Cognitive Map (FCM) and Deep Neural Network (DNN) algorithms. It was observed that the model depends on the chosen resampling technique. The dataset with numerical variables is available.

In [18], the authors built a model for the spread of hyperlipidemia and related factors in Shanxi Province. To construct the BN structure, the authors compared several algorithms, in particular MMPC-Tabu, Fast.iamb-Tabu and Inter.iamb-Tabu. To build the model, the authors use the Inter.iamb-Tabu hybrid algorithm. According to the model, it can be said that gender, BMI, and physical activity are directly related to hyperlipidemia. The accompanying materials provide the source code; the data is available on request.

Using logistic regression with univariate and multivariate models, the authors investigated the main correlates of cirrhosis complicated by encephalopathy (HE) [19]. Infection, electrolyte disorder and hepatorenal syndrome have been found to have a strong influence on the occurrence of HE. For evaluation, the authors used AUC (area under the receiver operating characteristic curve). For the reasoning model, they used deviations from the normal state of a person. The trained model is available in Appendix C in Figure C.2.

In [20], the authors predict mortality in patients after implantation of left ventricular assist devices. In addition to other factors influencing mortality, the model takes into account interventions in the last 48 hours. They compare the results of the BN model and HMRS. The model is available. Data is available upon request from the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) database.

Osteomyelitis (OM) is a bone infection that occurs more often in younger children. In [21], the authors used a BN to select the most appropriate antibiotic therapy based on data on the OM pathogen. The authors combine variance-based sensitivity analysis and expert surveys about certainty to identify the greatest influence on pathogen nodes. For validation the AUC was used. Data is not available.

Decisions in transplant care often involve trade-offs between potential benefit and potential harm of treatment or intervention. In [22], the authors build a model for making kidney transplant decisions. A decision-making

method based on Kidney Donor Risk Index (KDRI) was developed. The model predicts the probability of death over the next 3 years. Data is not available.

Assessing and managing the risk of violence is considered a critical component for decision making in medium secure services [23]. The researchers build a model in forensic psychiatry using a dataset referred to VoRAMSS. In order to find out the impact on the output node, sensitivity analysis is performed. The model is compared with other regression models trained on the same dataset. Data not available.

To assess and manage the risk of future violent re-offending for released prisoners with mental illness, a DSVM-P model was developed in [24]. The authors explore the issue of reducing the risk of future re-offending to an acceptable level by introducing interventions. Using sensitivity analysis applied to the interventions, the authors observe the most active symptoms. Data is not available.

A causally-based decision support tool for the management of violence risk among released prisoners using Bayesian networks was created in [25]. The risk analysis is managed and analysed through interventions on variables such as alcohol, drugs and psychiatric interventions. The model was compared with the results from HRC-20, VRAG and PCL-R risk assessment instruments. Data is not available. The process was replicated in [26]. The authors develop a risk management tool for discharged forensic prisoners using the same methodology. The model was compared with the results from HRC-20, SAPROF and PANSS risk assessment instruments. The data is not available.

Autism, or autism spectrum disorder (ASD), occurs due to developmental disorders caused by differences in the brain. For predicting autistic spectrum disorder, it is possible to use fuzzy cognitive maps (FCM) [27]. The authors used a non-linear hebbian learning for training model. In the study, experts, based on the constructed model, determine the boundaries for the acceptable probabilities of having autism. They define: definite autism, probable autism and no autism. The data is available.

A Bayesian network decision model was proposed for supporting the diagnosis of dementia, Alzheimers disease (AD), and mild cognitive impairment (MCI) [28]. In the paper the list of CDSS (clinical decision support system) was provided. The authors perform a sensitivity analysis for parameters like dementia, AD and mild cognitive impairment. The performance was tested by AUC, F1, MSE, MXE scores. The dataset based on data from the Duke University Medical Center and the Center for Alzheimer's Disease and Related Disorders can be purchased.

Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease, with a worldwide prevalence of 10.1% in people aged 40 years or older [29]. Using a Bayesian model, the authors analyse the impact of critical variables on the risk of rehospitalization in patients with COPD [30]. The authors argue that it is possible to reduce these risks with the help of personalised interventions. The accuracy of the model is determined in comparison with other machine learning methods. The dataset was constructed based on St. Mary's Hospital data.

In [31] and [32], the authors used machine learning (ML) techniques and built transplant survival models. For predicting the outcome of a heart transplant, the authors built a framework based on a BN model that can identify patient-specific survival risk scores and the interactions between the explanatory variables [31]. For testing performance of the model six evaluation metrics were used. The dataset was provided by United Network for Organ Sharing (UNOS). The dataset and software are available for download. Of the 119,873 organ transplants worldwide, 67% are kidney transplants, and 59% of those are from deceased donors, according to the World Health Organization [33]. A three-step Bayesian risk model for predicting graft survival in kidney transplantation was proposed in [32]. The UNOS data is used for building the model. The authors used several techniques, such as ANN (artificial neural network) and SVM (support vector machine), and sensitivity analysis for selecting features for the final dataset. For performance measure of the accuracy, sensitivity, specificity, f-measure, and g-mean metrics were used. Data is not available.

Approximately 537 million adults (20-79 years) are living with diabetes. The total number of people living with diabetes is projected to rise to 643 million by 2030 and 783 million by 2045 [34]. For the prevention of complications of type 2 diabetes mellitus (T2DM), the authors propose a model that predicts six complications of T2DM [35]. The model was built using the Tabu-search and Bootstrap algorithms. Data was taken from the National Health Clinical Center for the period 1st January 2009 to 31st December 2009. The authors compare the performance between BN, BN-wopi, NB, RF and C5.0 models using AUC, 95%CI, sensitivity and specificity metrics. The article also provides a comparative performance table of models from related studies by AUC score. Dataset is available on request.

In contrast, [36] proposes to predict the complications associated with type 1 diabetes. The paper presents two types of models using two different approaches (DDO-DBN, EI-DBN) in the design of the structure of the Dynamic Bayesian Network. The difference is that the second network is built on the basis of knowledge from the medical literature. As a result of the analysis, the authors determine threshold values for continuous variables. The authors used DCCT and EDIC data sets for building the model.

In [37], the possibility of automatic construction of the Bayesian network topology and ontology from electronic medical records using the K2 algorithm was studied. The dataset was built on the basis of 10,000 anonymized patient records. The classification performance of the constructed CBN is compared with other

inference models such as Naive Bayes, Basic, Random-node-input, and Frequency-based Bayesian networks. The data is available.

Infectious diseases are the world’s greatest killers, accounting for more than 13 million deaths annually among children and young adults alone [38]. Patients often self-medicate to treat infectious diseases. In such cases, a system is required that can help in the choice of antibiotics. In [39], the authors propose a system called IDDAP based on ontologies for infectious disease diagnosis and antibiotic therapy. The ontology system was built by combining existing ontologies. Performance analysis was carried out using ROC, and the system was tested on different ontologies. The ontology is available; the software has been removed from Github.

Non-communicable diseases (NCDs) kill 41 million people each year, equivalent to 71% of all deaths globally [40]. Prevention of these diseases can help in their development. In [41], the authors developed a system based on Bayesian networks. The system determines the impact of user interventions on the main risk factors. The task was to predict coronary heart disease. The desired health indications are also indicated, i.e. upper and lower limits of the normal state without complications. A number of datasets were used in this work; Pima Indians Diabetes Data Set is available on Kaggle.

While much attention has been paid to the problem of evaluating the effectiveness of therapy using observational data, little work has been done on evaluating the treatment effect of interventions [42]. In the paper, the authors propose a model that studies reducing the number of falls in elderly patients through interventions in the model. Data from 1810 patients at Lille University Hospital (France) are used to build models. Experiments were carried out with three prediction models (BN, SVM, and DT); BN structure and modalities are available.

There are a number of tasks in which it is required to make timely diagnostic and managerial decisions. One such challenge is diagnosing infections in children in the emergency department. Based on expert opinion and knowledge in the area of expertise, [43] developed a Bayesian model to predict the results of causative pathogens. The paper provides three clinical scenarios to support decision making by physicians. The model is available.

In [44], the authors identify factors associated with hypertension. To achieve this, they build a Bayesian network based on Tabu search. The study participants were selected only from cities in Shanxi province, which does not allow generalisation of the results to a wider population. For evaluation, the authors used accuracy, TPR, FPR, precision, recall and F-measure metrics using the Weka software. The model has parameters such as smoking or drinking that can be used as interventions. Dataset and model are available.

Finally, we remark that in Appendix B (see Tables 1 and 2) we summarise information on the availability of medical data. Data was collected through a systematic review of publications. In most papers, data from the UCI and Kaggle repositories are used. According to the analysis of papers, several articles were identified that met the criteria stated above. The case of interventions for fall prevention in elderly patients [42] was chosen as the best suited to further analysis.

Interventions and Disease Management: Risk Boundary Selection

In the medical field, prediction of the risk of disease requires establishing a statistical model of risk factors and diseases, and prediction of the probability of disease according to levels of multiple risk factors [45].

Usually, the reasoning about the risk boundaries is based on deviations from the normal state, as for example in [6], [19], [27], [46]. In the medical literature, there are also works which establish some limits/bounds on the observed variables that indicate the normal state of a patient, with values outside the limits indicating the presence of the disease. This section provides several examples of such works.

Some articles have outlined specific risk boundaries [14], [15],[31], [32], [41], which can be used to evaluate interventions and, therefore, to recommend more effective personal therapy.

In [32], the authors set boundaries for the response to transplantation. There are three risk groups defined: low, medium and high risk. Depending on which risk group a patient falls in, it is possible to choose personalized treatment more accurately, and, more importantly, to prevent a patient from falling into a high-risk category in advance, by determining the influence of certain factors on risk.

In [41] interval boundaries are indicated for CAD risk factors. Also in this work, the authors provide a comparative analysis of similar approaches, comparing them in terms of parameters of risk factors analysis and context awareness. Based on the model, the authors developed an application that provides recommendations on factors that can exacerbate or alleviate the course of the disease. To do this, they created several scenarios and tested the system on two datasets.

An alternative to using boundaries is finding the most optimal solution using influence diagrams, i.e., a Bayesian network augmented by utility nodes (UN).

The authors of [22] suggest using the Kidney Donor Risk Index (KDRI) to evaluate complex transplant decisions. The metric assesses the risk of transplant rejection compared to a 40-year-old healthy donor. The model was built in Netica using UN. The purpose of using utility nodes is to maximize the expected value while looking for the most optimal solution.

Regarding acceptable levels of numerical variables, [46] presents an algorithm for the treatment of diseases associated with psoriasis. For example, for the treatment of metabolic syndrome, levels are set for HDL, AHT, BP, and TG. Using the reasoning model of this work as an example, experts can build BN models, determine acceptable levels of variables, and design effective interventions.

In [47], algorithms for the diagnosis of testosterone deficiency and follow up of testosterone therapy are developed. From analysis of the literature, the authors identify the main symptoms, signs, and conditions indicative of testosterone deficiency. The levels of physical indicators are also given. The information provided in the article can be used to design intervention-based CDSS.

In an infection control program studying the implementation of preventive measures, the use of data and surveillance audits is central. To improve these practices, a list of interventions can be compiled based on CDC recommendations and practice monitoring [48]. This work provides recommendation guidelines for the prevention, diagnosis, and management of Hepatitis C (HCV) in patients with chronic kidney disease (CKD). The paper presents treatment schemes and risk grade for CKD, which can be used as a definition of acceptable boundaries of the target node and effective interventions.

Interventions can also be derived from literature analysis, as was done in [49]. As a result of the analysis, the authors proposed pharmacological and non-pharmacological interventions for BPSD (dementia symptoms).

Based on the works presented in this section (and similar other works), it is possible to develop more effective systems for controlling risk levels based on interventions, which can be the next step in building effective CDSS systems.

Review Summary and Model Selection

In most of the analyzed papers, machine learning methods like support vector machines (SVM), Bootstrap Forest (BF), Bayesian belief network (BBN), and artificial neural networks (ANN) were used. When BN models are used, they may be part of a larger pipeline [31] if the data was not initially prepared/in the right format to work with BNs. AUC is most commonly used for accuracy evaluation. Bayesian network models are mostly built on the basis of expert opinions [43], but sometimes they are also built using the K2 [37] or TabuSearch [18] algorithms, then checked or supplemented by experts [42]. These authors use their own data derived from close cooperation with medical institutions (Table B1 of Appendix B) or data from repositories (Table B2) or medical databases (Table B3). Also, in some works, data from multiple sources can be combined if incomplete [41]. By interventions, the authors mostly refer to medical interventions that are already accounted for in the Bayesian network [39]. In some works, sensitivity analysis is carried out to determine the impact of various factors on the target node [16], [31] according to some machine learning classifier. Similarly, it is possible to use ‘what-if analysis’ in Bayesian networks to discern the effect of a given variable on the target by conditioning on the value of that variable [32]. This could be used as a heuristic for selecting promising interventions to study. The main evaluation indices of a BN model are true positive rate (TPR), true negative rate (TNR), recall, and precision. Sensitivity (TPR) indicates the proportion of positive classes correctly predicted and the ability of the BN to recognize positive classes. Specificity (TNR) represents the proportion of correctly predicted negative classes and measures the ability of the BN to recognize negative classes [44].

In Table B1 (Appendix B), the found models are highlighted in green, and the proposed model for our experimental study of interventions is highlighted in blue (a shorter dataset was attached to the work). Appendix C contains the constructed models based on the available data in the papers.

Experimental Evaluation

This section of the report summarises our experiments on selected models using the software tool developed in [1]. Our workflow was primarily based upon the framework/pipeline illustrated in Appendix D for Bayesian network modelling, based on [50]. In the following experiments, since we already have access to the Bayesian network from the literature, we skipped the first few steps. For interventional modelling, we make use of the IntRob (interventional robustness) software [1], based on a recently proposed approach to providing guarantees on the effects of combinations of interventions. As we will see, this is important for providing safety guarantees with respect to different treatment (intervention) policies.

We identified the Bayesian network models from [14, 15, 42] as particularly suitable for interventional analysis; in particular, we conduct experiments on the basis of the model from paper [14]. In this paper, the authors attempt to identify patients at risk for lymph node metastasis (LNM) in endometrial cancer. The Bayesian network model can be used to predict lymph node metastasis, as well as outcomes such as patient survival up to 5 years and recurrence of disease, given some (incomplete) evidence/information about the patient.

An oncologist treating a cancer patient employs the following procedure. In the first stage, a diagnosis is made and it is determined how much the tumor has spread and whether the patient is operable. In the second

stage, if the patient is operable, then they apply radiation therapy targeting the tumor and nearby tissues (this depends on many factors). After irradiation, the patient is surgically operated on, with irradiated and nearby tissue removed. Finally, chemotherapy is prescribed to prevent spread of tumour cells into lymph nodes or blood.

In their work, the authors focus on predicting lymph node metastasis, which is one of the most important prognostic factors for patient outcomes, and which can be significantly influenced by adjuvant therapy: it is thus of significant practical interest to be able to predict LNM in order to inform therapy decisions. We begin by performing feature selection for the classifier based on their impact on the LNM probability in the Bayesian network. In Table 1, we show the probability of LNM and probability of LVSI (lymph-vascular space invasion), for a range of different evidence values. The green cells are updated values and the blue one was chosen for classification.

Table 1. Probability estimates for lymph node metastasis and LVSI given different evidence [14]

Evidence provided to the Bayesian network	Modalities	Lymph node metastasis	LVSI
No evidence		8.6	16
Preoperative grade	1	4.7	10.6
	2	8.2	14.6
	3	20.7	34.4
Preoperative grade, L1CAM	1,negative	3.9	9.9
	1,positive	17.7	22
	2,negative	6.6	13.1
	2,positive	28.2	28.1
	3,negative	17.4	31.8
	3,positive	30.4	41.8
Preoperative grade, ***PM	1,favorable*	2.8	8.9
	1,unfavorable**	35.8	45
	2,favorable	5.1	11.6
	2,unfavorable	36.2	43.4
	3,favorable	16.9	29.3
Preoperative grade, Ca-125	3,unfavorable	37.1	45.4
	1,normal	1.5	8.9
	1,elevated	22.8	20.3
	2,normal	2.8	11.8
	2,elevated	34.7	28.2
	3,normal	7.7	28.5
	3,elevated	60.9	52.2

*Favorable: all IHC stainings were normal (ER, PR positive, L1CAM negative, p53 wildtype).

**Unfavorable (ER, PR negative, L1CAM positive, p53 mutant). Ca-125, cancer antigen 125; ER, estrogen receptor; L1CAM, L1 cell adhesion molecule; PR, progesterone receptor.

***PM - molecular profile.

In Table 2, we show a classification of risk groups for LNM.

Table 2. LNM risk table [14]

Predicted probability	Risk group
< 1%	Very low
1%-5%	Low
6%-15%	Intermediate
16%-25%	High-intermediate
> 25%	High

According to Table 1, the following variables were selected as features for the classifier: ER, PR, L1CAM, p53, preoperative grade, CA125. We used a threshold of 0.05 for the prediction of LNM, in accordance with

the risk profiles in Table 2. We use the BNC.SDD software to obtain a logical representation of the resulting Bayesian network classifier (BNC), which we use for further analysis in the IntRob software.

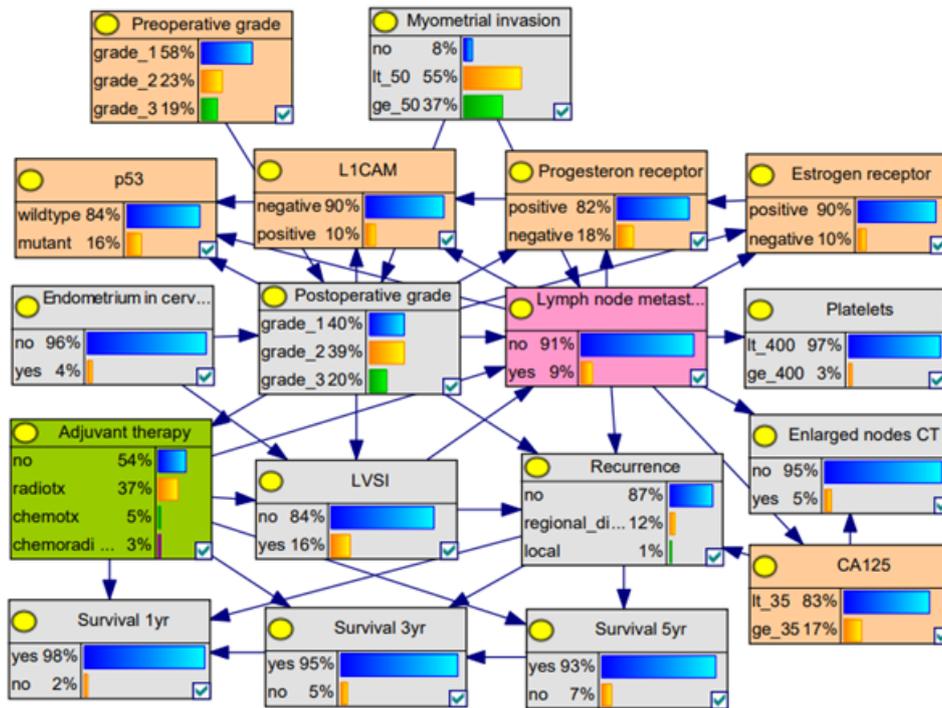


Fig. 1 The chosen Bayesian network. The target node (LNM) is shown in pink. Yellow nodes was chosen as features for classification, while green nodes represent intervention targets.

```
{
  "id": "1",
  "name": "C4",
  "filetype": "net",
  "vars": 6,
  "root": "LNM",
  "leaves": ["ER", "PrimaryTumor", "PR", "L1CAM", "p53", "CA125"],
  "threshold": 0.05,
  "input_filepath": "networks/",
  "output_filepath": "output/"
}
```

Fig.2 JSON file for LNM classifier

For our first experiment, we considered the probability of LNM under interventions on adjuvant therapy. Such an intervention represents a change in treatment policy; it can be seen, in particular, that adjuvant therapy has a causal influence on LNM from the Bayesian network graph. In particular, we asked the following question: what are the potential consequences of instituting a bad treatment policy? To analyze this, we used the IntRob software to compute an upper bound on the probability of lymph node metastasis, under all possible interventions (treatment policies). In Figure 5, we see that the worst-case policy may result in 60% of patients suffering metastasis, up from 9% under the current policy. This shows that it is vital to choose the right adjuvant therapy for each patient depending on their characteristics, and failing to do so can be unsafe. In Figure 6, we conducted another test to see how different interventions on adjuvant therapy affect the false negative rate of the trained classifier; that is, whether this might result in the classifier mispredicting patients as not at risk of LNM when they actually are. Interestingly, the classifier is surprisingly robust, with a false negative probability of only 0.001. This can possibly be attributed to the fact that the classifier uses indicators causally downstream from LNM (p53, L1CAM, etc.), which provide sufficient information to correctly predict LNM, even with the shift observed above in the LNM distribution.

The results of the working of IntRob software can be seen in Figures 3-5.

```

av@av-VirtualBox: ~/work/Interventional-robustness
av@av-VirtualBox:~/work/interventional-robustness$ bash obtain_joint_cnf.sh -n models/C4.net -d C4
_1.odd -m config_C4.txt -o output -t
Creating Bayesian Network CNF...

DIMACS CNF written to: output/bn.cnf

Done
Adjusting Constraints...
0 0
Done
Converting Decision Function to CNF...
Done
Combining BN and DF CNF...
Done

```

Fig. 3 First four steps of the IntRob algorithm

```

av@av-VirtualBox:~/work/Interventional-robustness$ ./c2d_linux -in output/combined.cnf -dt_method 3

c2d compiler version 2.20
Copyright (c) Automated Reasoning Group, UCLA 2004-2005
Licensed only for non-commercial, research and educational use

Loaded cnf: 655 vars 768 clauses (0 eclauses)
0 unit clauses, 161 binary clauses, max clause size: 6
Generating dtree... done.
Max Cluster=18, Cutset=3, Context=17, Separator=13, Height=96
Compiling...done.
Cache memory: 0.1 MB / Cache count: 1276
NNF memory: 0.2 MB
Learned clauses: 0
Compile Time: 0.040s / Pre-Processing: 0.006s / Post-Processing: 0.005s

0.9% of nodes, and 1.0% of edges are dead.
Saving 5676 nodes and 16842 edges...done.

Total Time: 0.054s
av@av-VirtualBox:~/work/Interventional-robustness$

```

Fig. 4 c2d compiler output

```

av@av-VirtualBox: ~/work/Interventional-robustness/bounding/bin
av@av-VirtualBox:~/work/interventional-robustness/bounding/bin$ java ace.UpperBound config_C4.txt
INTROB UB: 0.5914168769574432
av@av-VirtualBox:~/work/interventional-robustness/bounding/bin$

```

Fig. 5 Upper bound on LNM probability under worst-case intervention

```

av@av-VirtualBox: ~/work/Interventional-robustness/bounding/bin
av@av-VirtualBox:~/work/interventional-robustness/bounding/bin$ java ace.UpperBound config_C4.txt
INTROB UB: 0.0010899767077083176
av@av-VirtualBox:~/work/interventional-robustness/bounding/bin$

```

Fig. 6 Upper bound on false negative probability

For the second experiment, we study the probability of recurrence, again under interventions to the adjuvant therapy. Applying the IntRob software to derive the worst-case probability of recurrence over all possible interventions, we find in Figure 8 that the probability of (regional-distant) recurrence can reach as high as 38%, once again demonstrating the risks of inappropriate treatment.

```

av@av-VirtualBox:~/work/interventional-robustness$ bash obtain_joint_cnf.sh -n models/C4.net -d odd/C4_e2.odd -m config_C4_2.txt -o output -t
Creating Bayesian Network CNF...

DIMACS CNF written to: output/bn.cnf

Done
Adjusting Constraints...
0 0
Done
Converting Decision Function to CNF...
Done
Combining BN and DF CNF...
Done
av@av-VirtualBox:~/work/interventional-robustness$ ./c2d_linux -in output/combined.cnf -dt_method 3

c2d compiler version 2.20
Copyright (c) Automated Reasoning Group, UCLA 2004-2005
Licensed only for non-commercial, research and educational use

Loaded cnf: 621 vars 665 clauses (0 eclauses)
0 unit clauses, 92 binary clauses, max clause size: 6
Generating dtree... done.
Max Cluster=18, Cutset=1, Context=17, Separator=13, Height=90
Compiling...done.
Cache memory: 0.1 MB / Cache count: 1588
NNF memory: 0.2 MB
Learned clauses: 0
Compile Time: 0.043s / Pre-Processing: 0.005s / Post-Processing: 0.005s

0.9% of nodes, and 1.0% of edges are dead.
Saving 6385 nodes and 20715 edges...done.

Total Time: 0.060s

```

Fig. 7 IntRob software for second experiment

```

av@av-VirtualBox:~/work/interventional-robustness/bounding/bin$ java ace.UpperBound config_C4_2.txt
INTROB UB: 0.37710775935220886

```

Fig. 8 Upper bound on recurrence probability under worst-case intervention

Finally, for the last experiment, we considered 5-year survival ('Survival 5yr'). We performed a sensitivity analysis in Figure 9 according the framework in Appendix D, to find relevant features to use for the classifier. Based on this, we trained a classifier using the following nodes/features: PrimaryTumor, CA125, Therapy, Recurrence. The input file for the ODD compiler is shown on Figure 10.

We now consider how 5-year survival can be improved using interventions. In Figure 13, we use the IntRob software to assess the maximal probability of 5-year survival, under all possible interventions to recurrence and adjuvant therapy. We find in Figure 13 that the upper bound on this probability is 1 (up to floating point error), indicating that there may be significant room for improvement of patient outcomes by improving treatment policies and reducing recurrence.

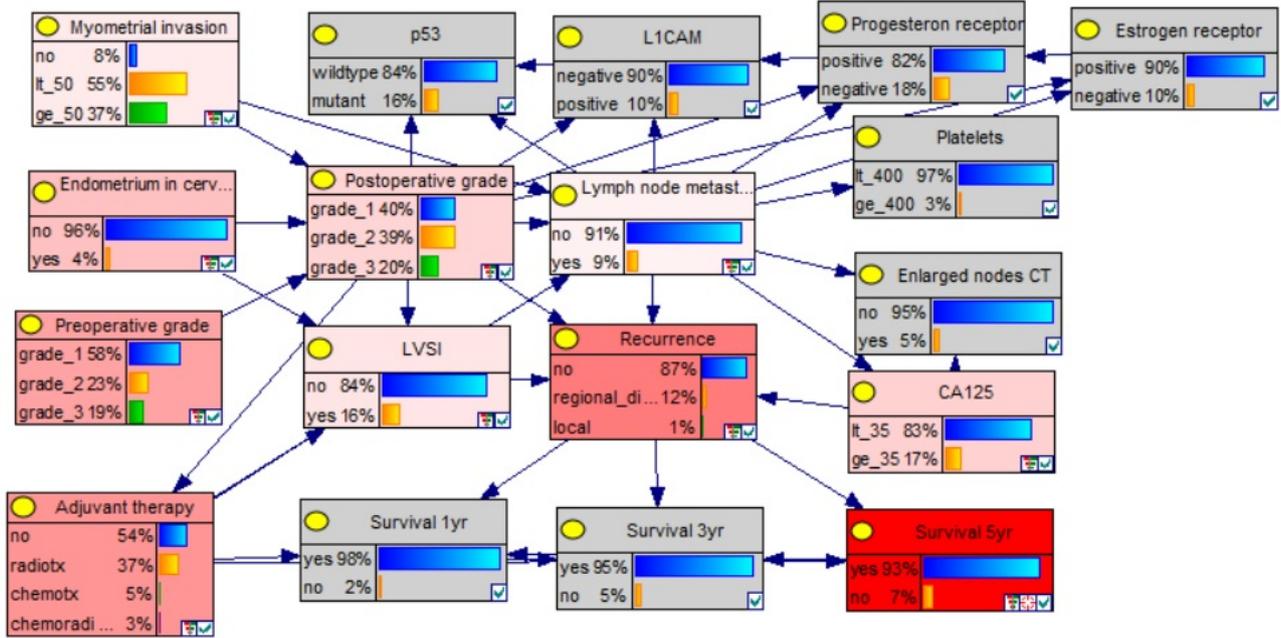


Fig. 9 Sensitivity analysis

```
{
  "id": "1",
  "name": "C4",
  "filetype": "net",
  "vars": 4,
  "root": "Survival5yr",
  "leaves": ["PrimaryTumor", "CA125", "Therapy", "Recurrence"],
  "threshold": 0.5,
  "input_filepath": "networks/",
  "output_filepath": "output/"
}
```

Fig. 10 JSON config file for 5-year survival classifier

The output file after compiling in BNC_SDD software is shown in Figure 11.

```
[PrimaryTumor, Therapy, CA125, Recurrence]
3 3 S1 S1 S1
2 2 3 3
1 1 2 2 2 2
0 0 1 1 1
```

Fig. 11 ODD file for 5-year survival classifier

```

av@av-VirtualBox:~/work/interventional-robustness$ bash obtain_joint_cnf.sh
-n models/C4.net -d C4_1.odd -m config_C4_5.txt -o output/ -t
Creating Bayesian Network CNF...

DIMACS CNF written to: output//bn.cnf

Done
Adjusting Constraints...
0 0
Done
Converting Decision Function to CNF...
Done
Combining BN and DF CNF...
Done
av@av-VirtualBox:~/work/interventional-robustness$ ./c2d_linux -in output/co
mbined.cnf -dt_method 3

c2d compiler version 2.20
Copyright (c) Automated Reasoning Group, UCLA 2004-2005
Licensed only for non-commercial, research and educational use

Loaded cnf: 618 vars 658 clauses (0 eclauses)
0 unit clauses, 87 binary clauses, max clause size: 6
Generating dtree... done.
Max Cluster=19, Cutset=1, Context=19, Separator=13, Height=90
Compiling...done.
Cache memory: 0.1 MB / Cache count: 598
NNF memory: 0.1 MB
Learned clauses: 0
Compile Time: 0.017s / Pre-Processing: 0.005s / Post-Processing: 0.006s

0.8% of nodes, and 1.0% of edges are dead.
Saving 3138 nodes and 5924 edges...done.

Total Time: 0.032s
av@av-VirtualBox:~/work/interventional-robustness$

```

Fig. 12 IntRob software for the final experiment

```

av@av-VirtualBox:~/work/interventional-robustness/bounding/bin$ java ace.UpperBound
config_C4_5.txt
INTROB UB: 1.0000004518375285
av@av-VirtualBox:~/work/interventional-robustness/bounding/bin$ █

```

Fig. 13 Upper bound on 5-year survival probability under best-case intervention

In conclusion, our analysis has revealed a number of insights into the Bayesian network model. The obtained BN bounds can be utilised to develop subsequent treatments strategies, as well as used as input into models that improve QoL or QoL [8] or facilitate EOL at home [9]. It is also possible to use medical protocols that reduce the likelihood of falling into a certain group.

Acknowledgements

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Appendix A

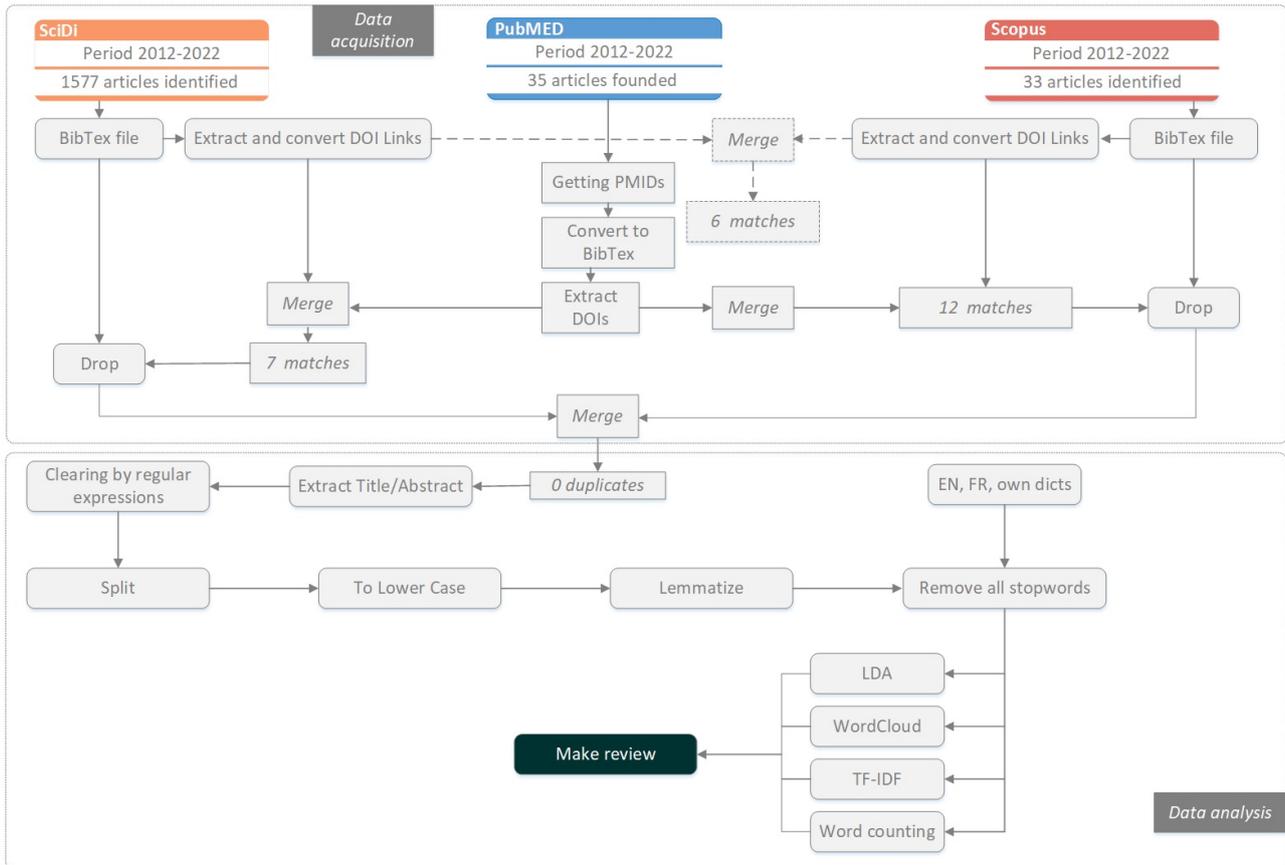
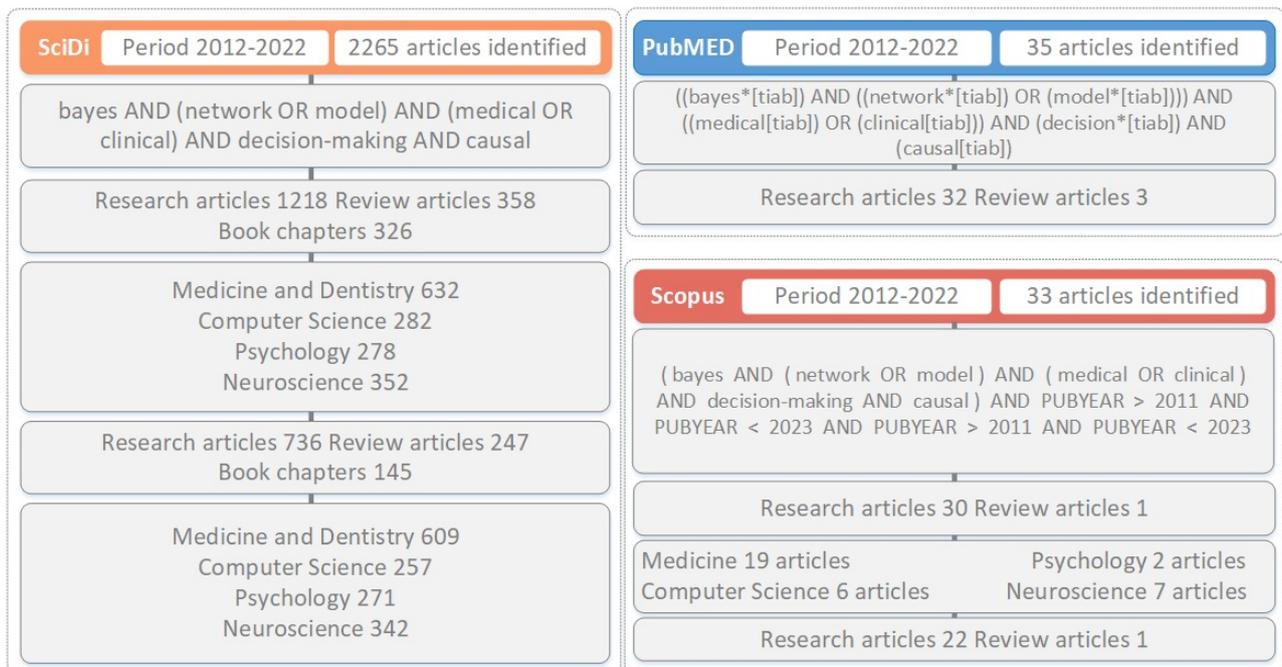


Fig. A1 Research algorithm



accessed 4.08.22

Fig. A2 Articles identified

100 most common tokens: ('study', 922), ('model', 855), ('data', 816), ('patient', 806), ('risk', 682), ('method', 650), ('result', 579), ('clinical', 525), ('research', 507), ('disease', 490), ('health', 459), ('analysis', 423), ('factor', 379), ('learning', 374), ('decision', 370), ('approach', 366), ('system', 358), ('network', 357), ('associated', 356), ('treatment', 354), ('outcome', 344), ('based', 335), ('review', 325), ('effect', 317), ('evidence', 311), ('process', 286), ('information', 284), ('brain', 277), ('finding', 275), ('year', 270), ('level', 268), ('care', 258), ('group', 251), ('support', 247), ('development', 247), ('social', 239), ('however', 237), ('different', 235), ('control', 232), ('new', 228), ('knowledge', 227), ('paper', 227), ('disorder', 224), ('individual', 223), ('framework', 219), ('conclusion', 217), ('provide', 217), ('rate', 213), ('performance', 210), ('two', 208), ('bayesian', 206), ('change', 206), ('task', 205), ('event', 205), ('population', 203), ('prediction', 199), ('increased', 196), ('cognitive', 195), ('feature', 192), ('behavior', 192), ('time', 191), ('participant', 190), ('current', 189), ('relationship', 188), ('measure', 186), ('trial', 184), ('role', 183), ('causal', 183), ('machine', 181), ('including', 181), ('people', 180), ('intervention', 180), ('potential', 180), ('one', 180), ('literature', 179), ('child', 177), ('medical', 176), ('high', 173), ('across', 173), ('within', 172), ('association', 172), ('impact', 170), ('symptom', 170), ('area', 169), ('mechanism', 169), ('technique', 168), ('human', 168), ('present', 167), ('show', 166), ('compared', 166), ('neural', 165), ('proposed', 164), ('response', 164), ('problem', 161), ('assessment', 161), ('function', 160), ('cause', 160), ('higher', 159), ('mortality', 159), ('could', 158)

TF-IDF OUTPUT:

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Fig. A3 Bag of worlds output

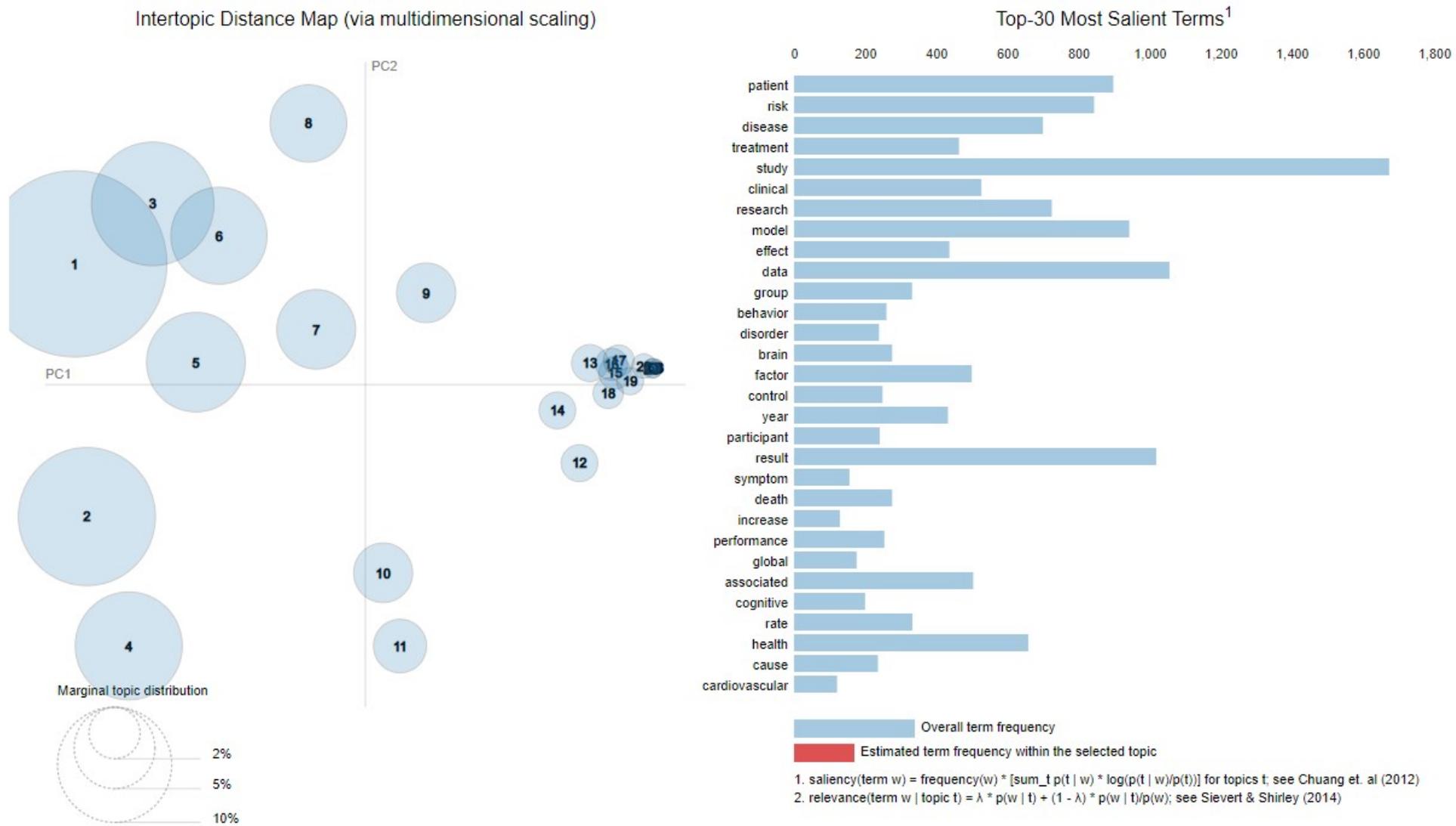


Fig. A4 LDA

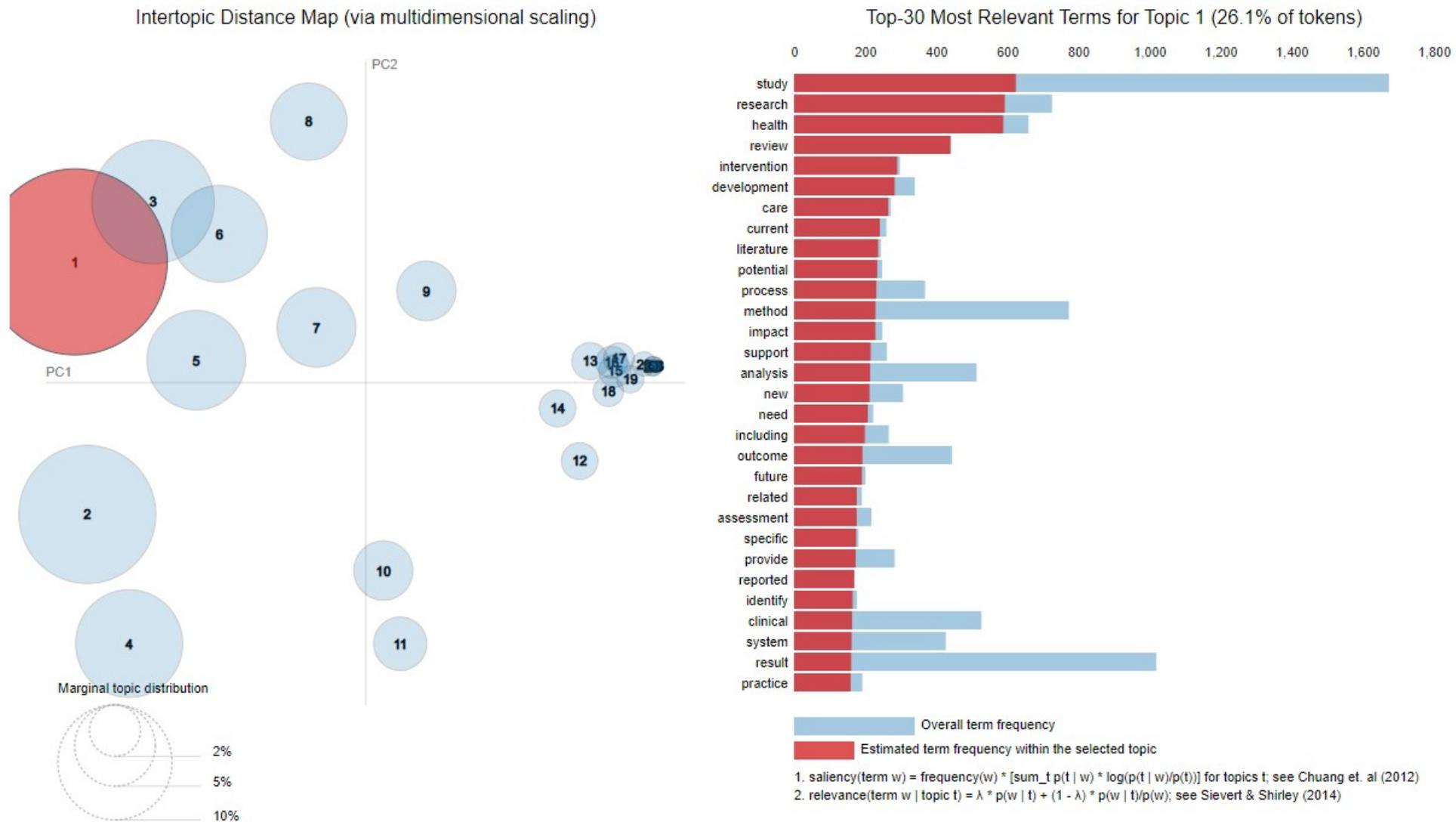


Fig. A4 LDA

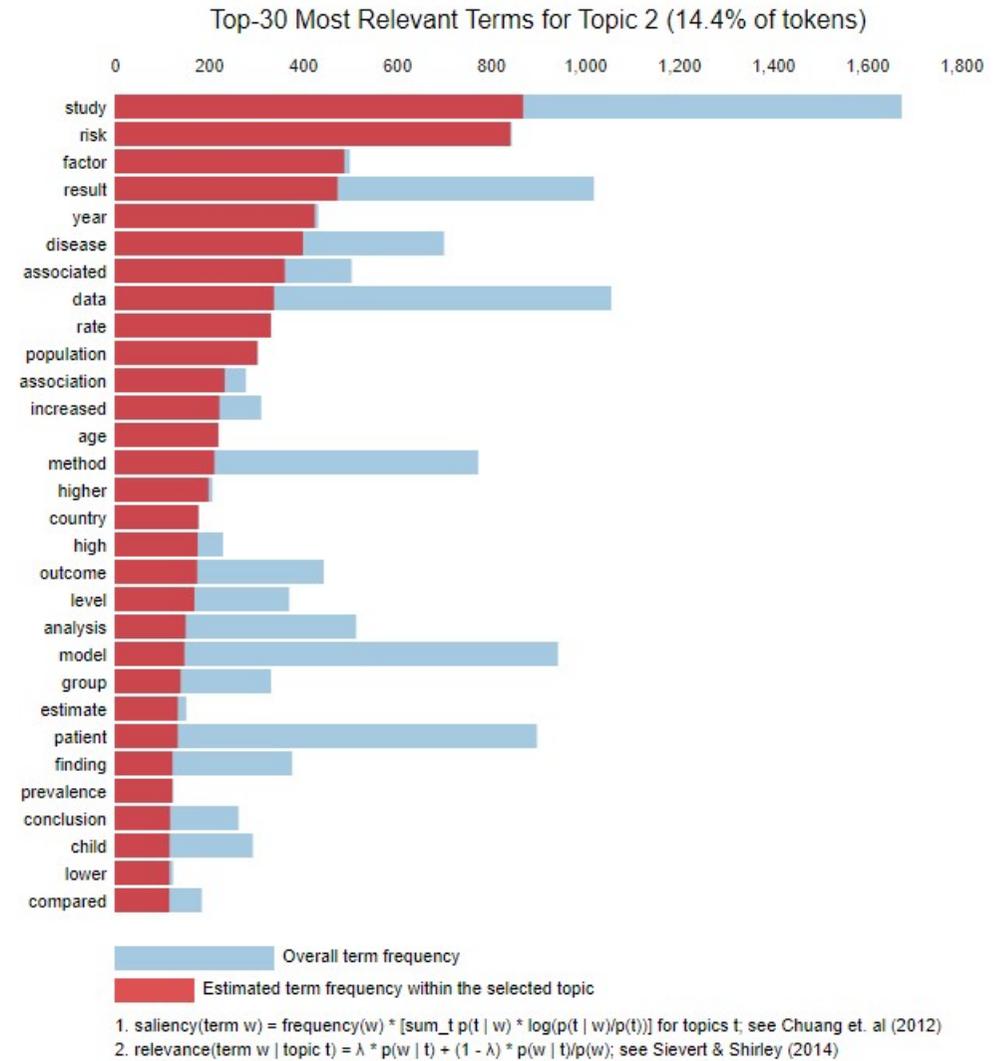
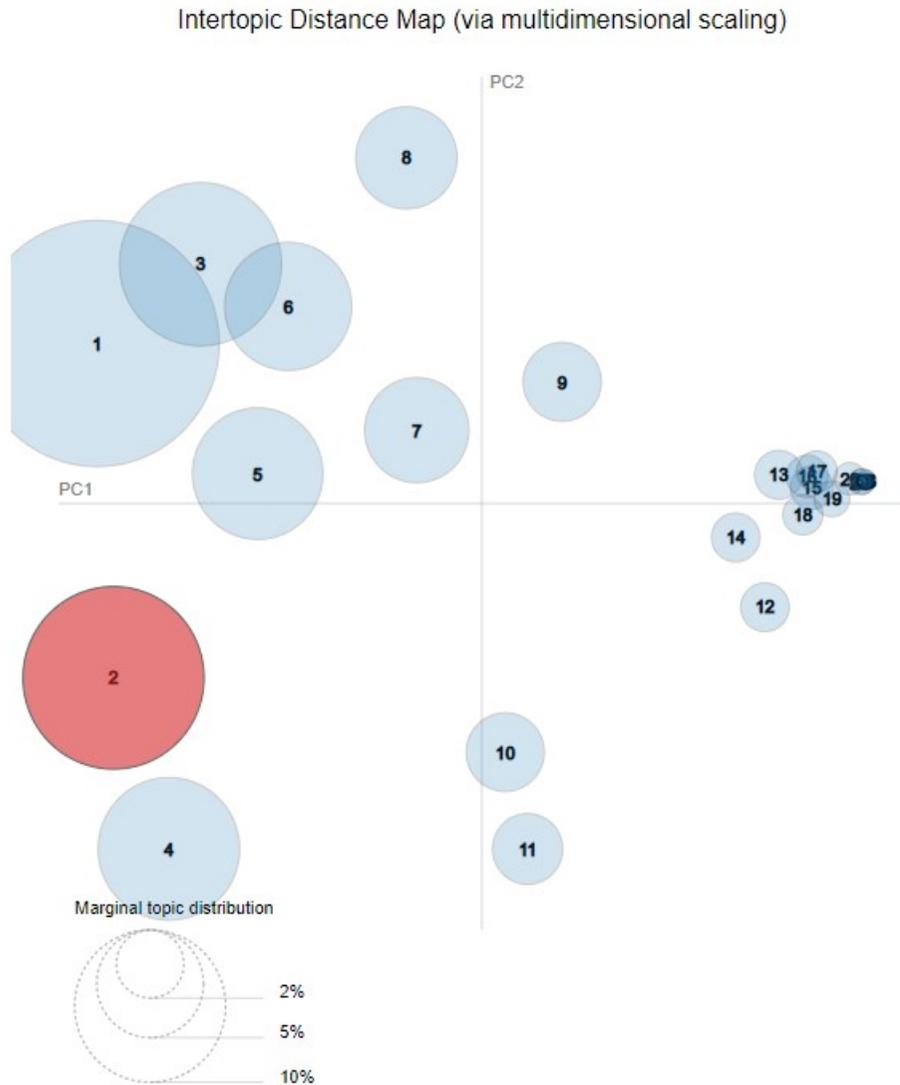


Fig. A5 LDA

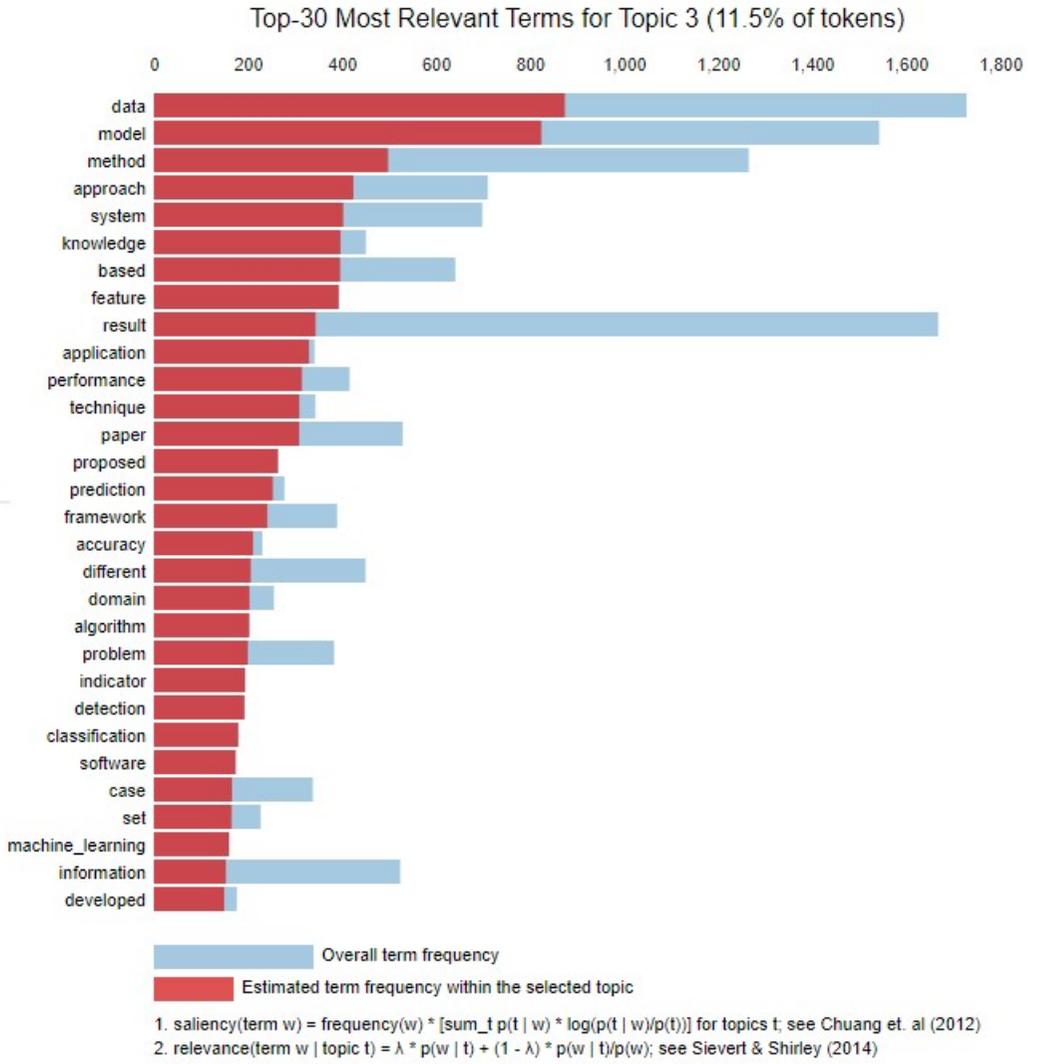
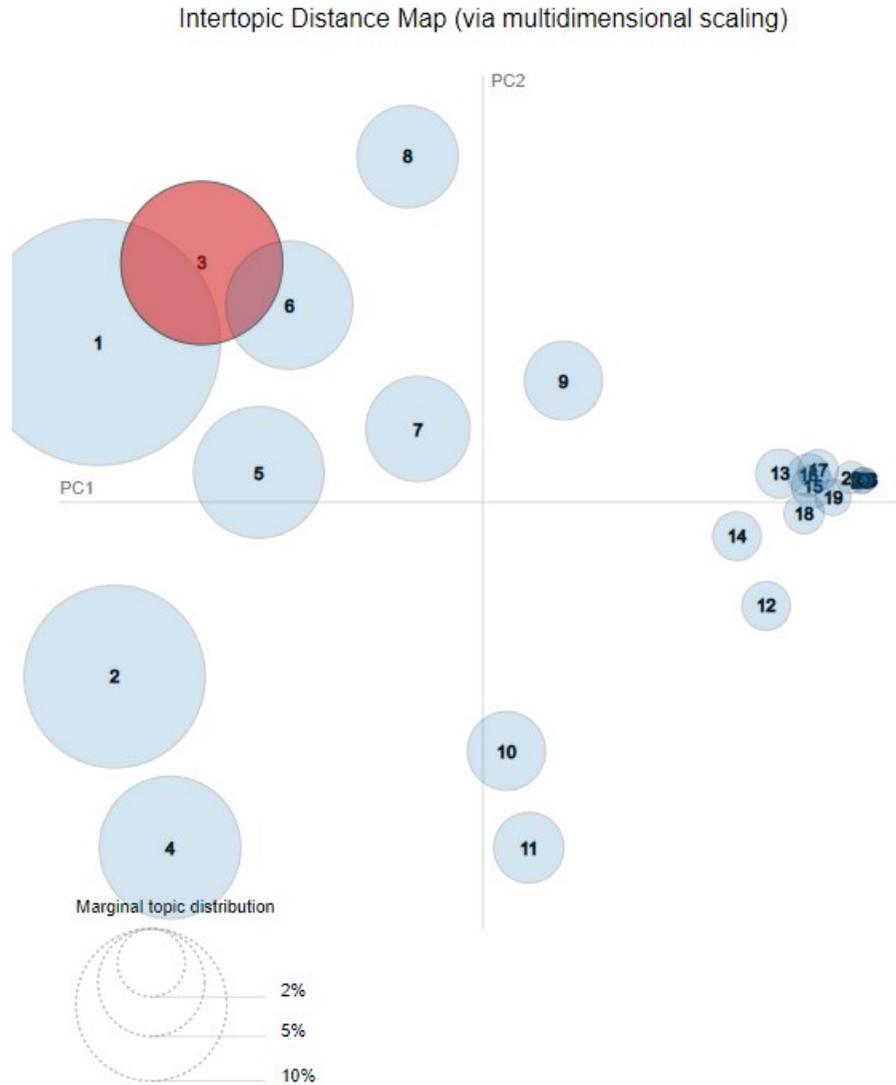


Fig. A6 LDA

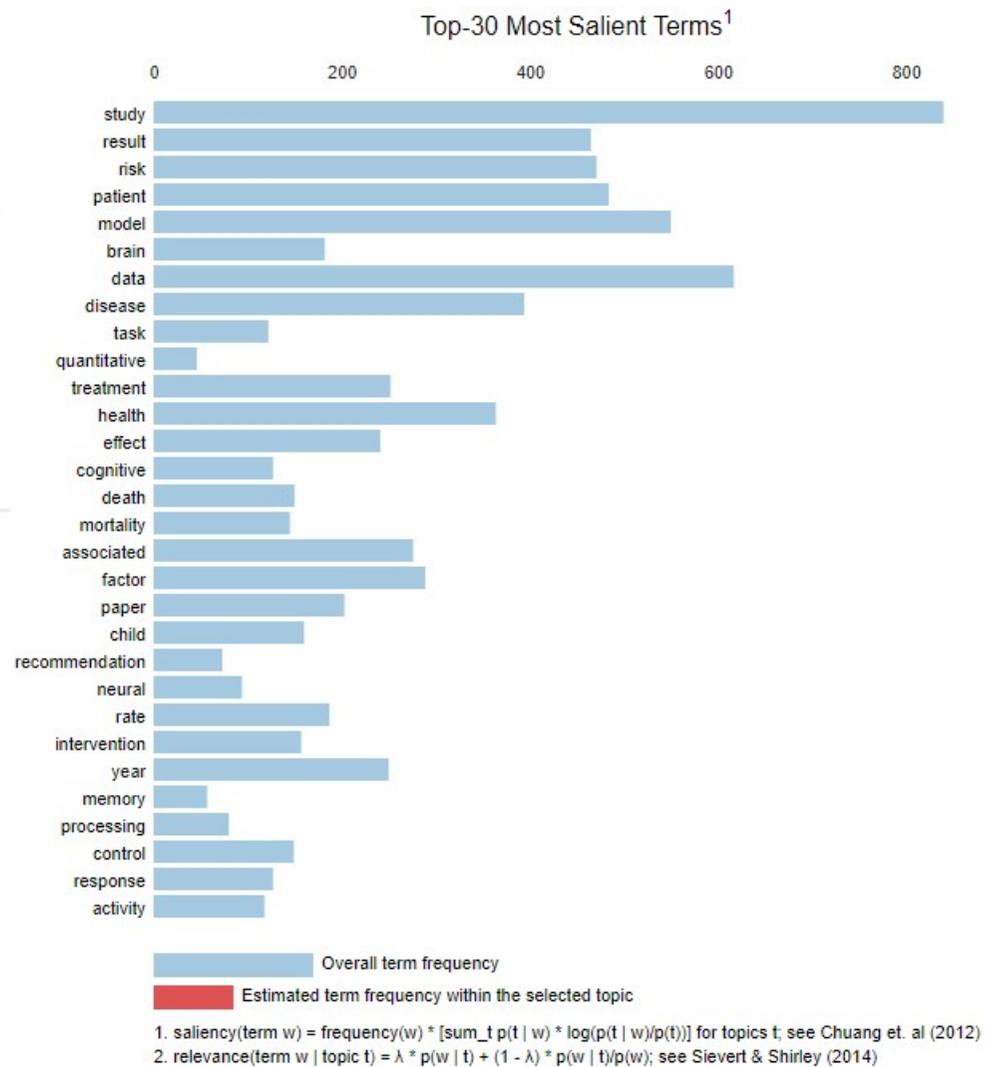


Fig. A7 LDA

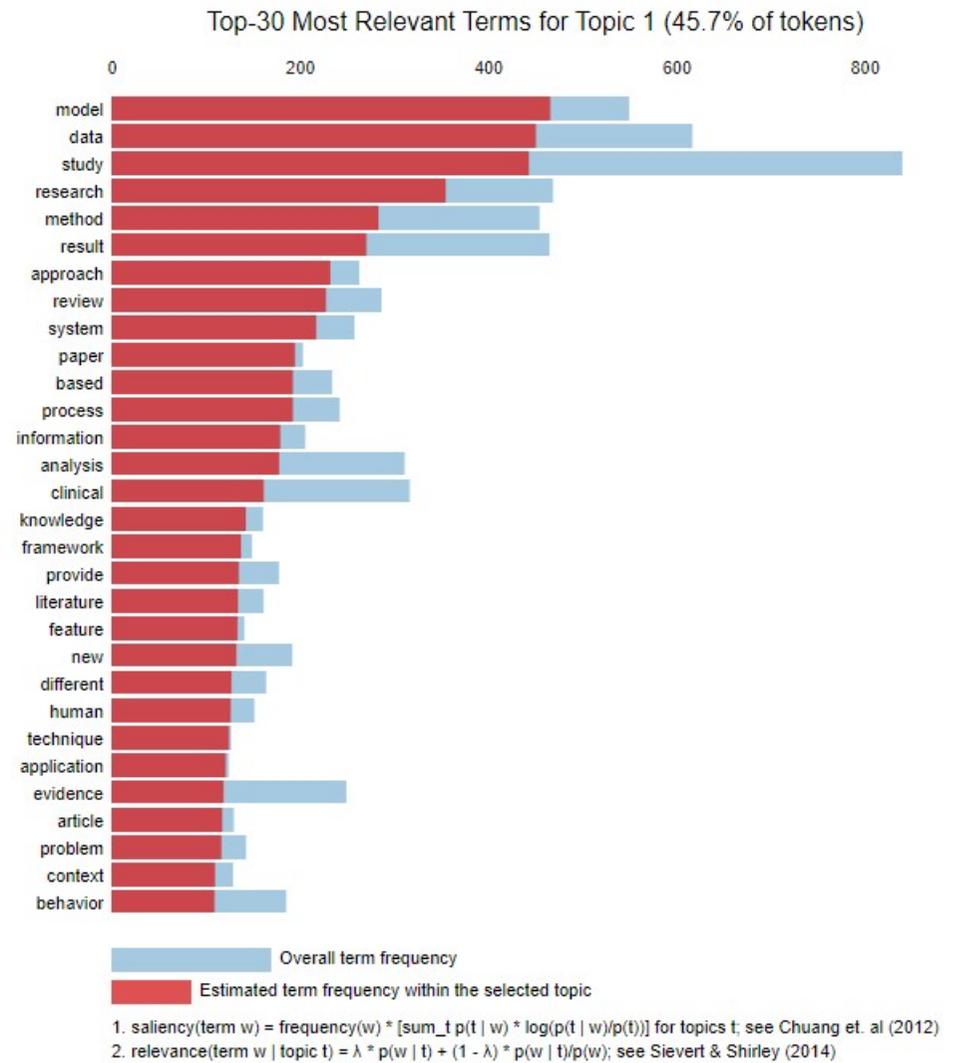
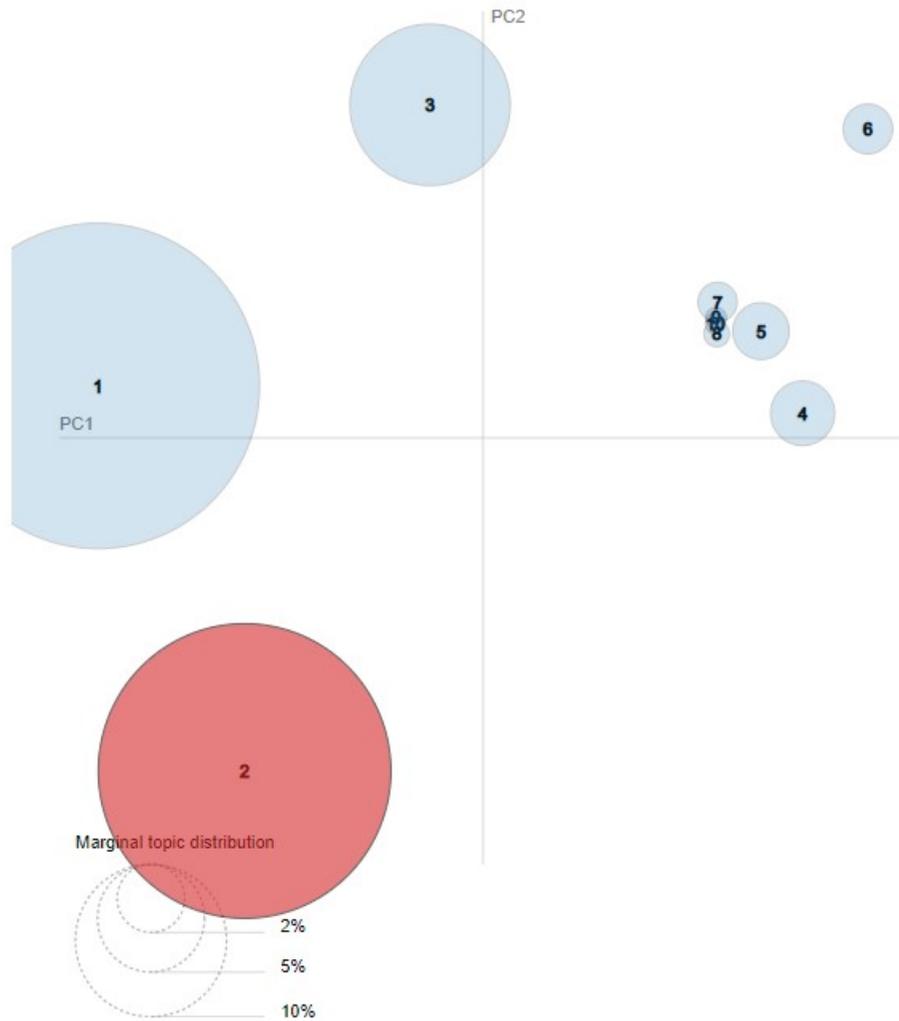
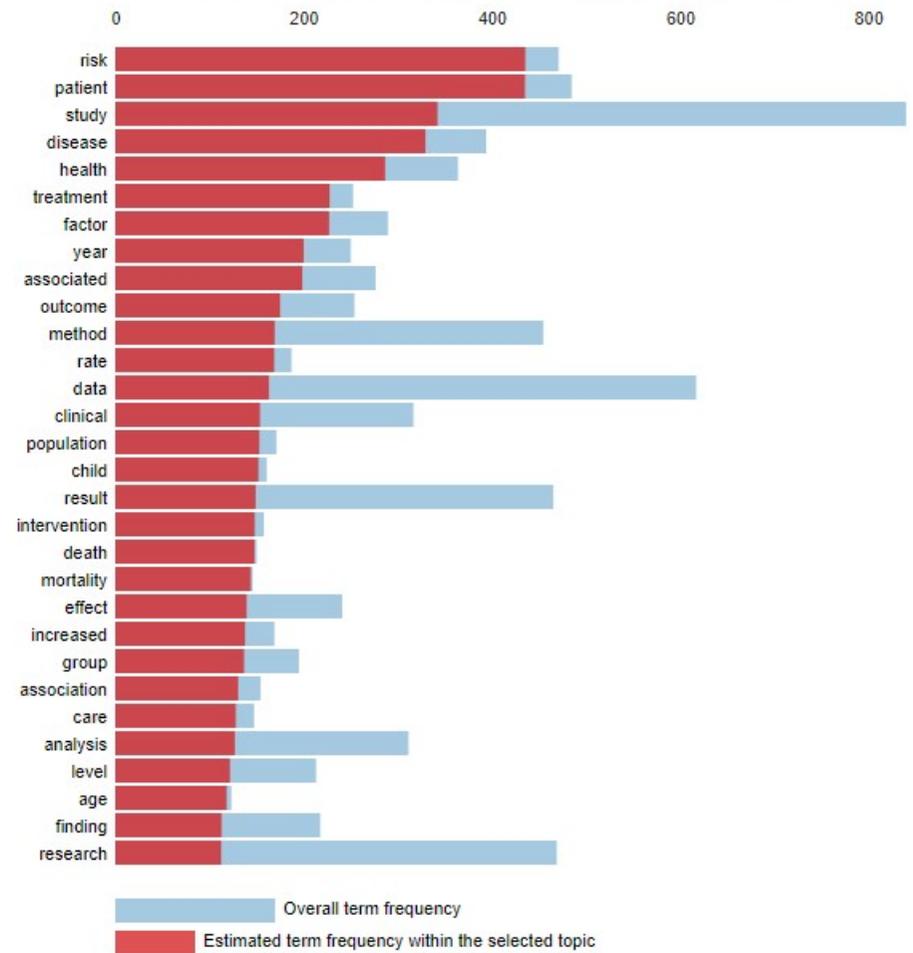


Fig. A7 LDA

Intertopic Distance Map (via multidimensional scaling)



Top-30 Most Relevant Terms for Topic 2 (37.5% of tokens)



1. saliency(term w) = frequency(w) * [sum_t p(t | w) * log(p(t | w)/p(t))] for topics t; see Chuang et. al (2012)
 2. relevance(term w | topic t) = λ * p(w | t) + (1 - λ) * p(w | t)/p(w); see Sievert & Shirley (2014)

Fig. A8 LDA

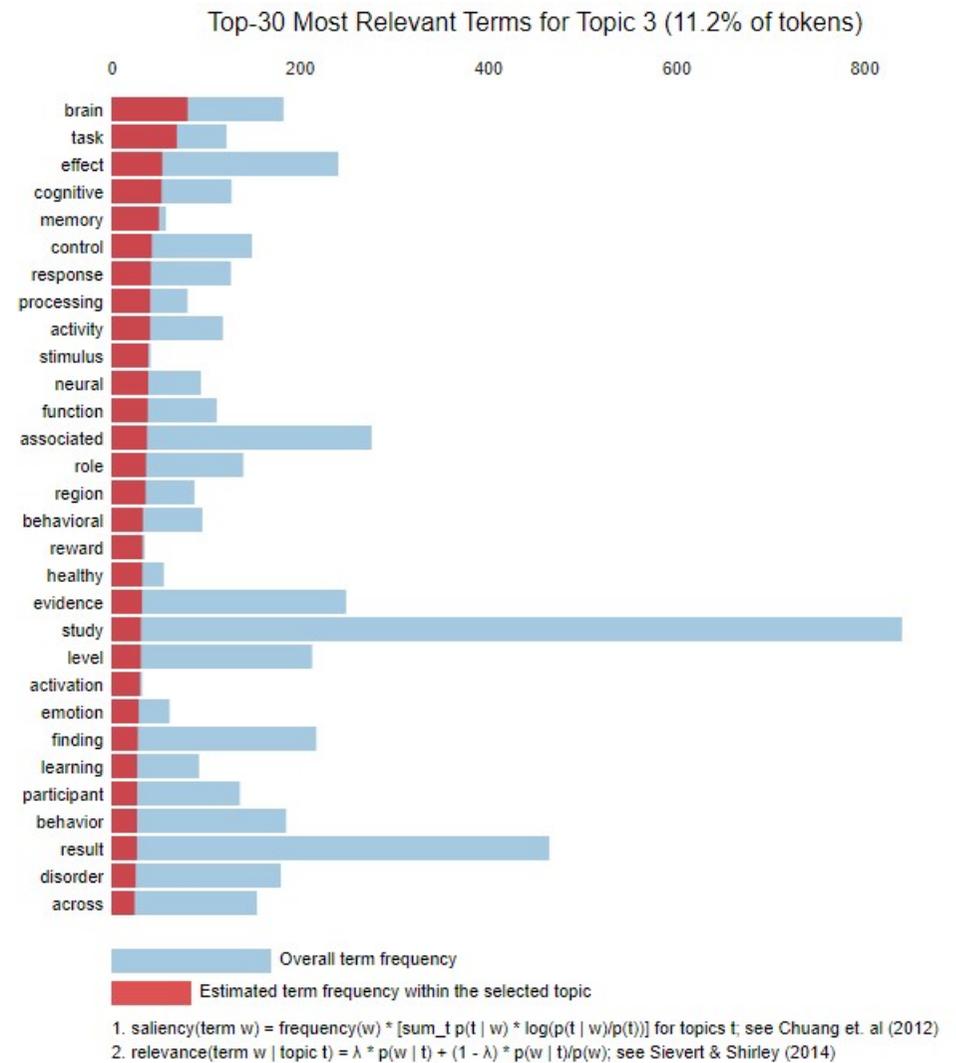
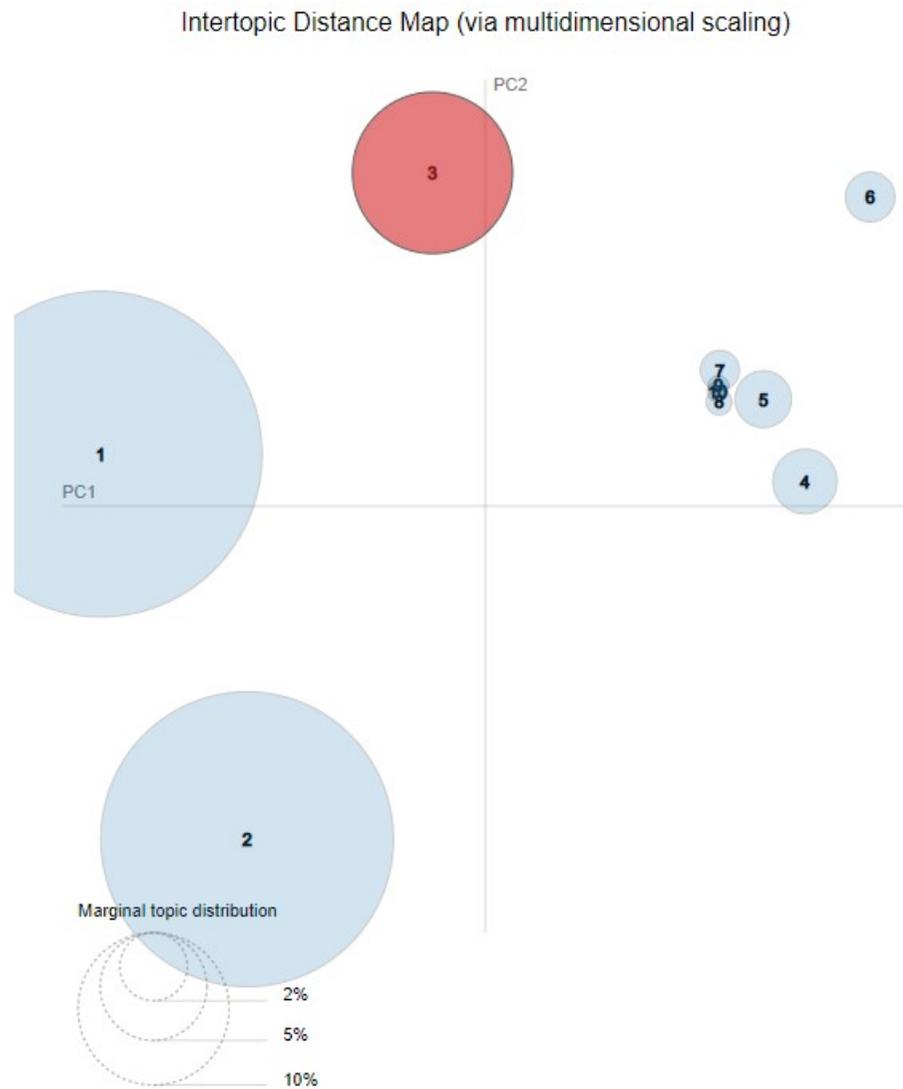


Fig. A9 LDA

Appendix B

Table 1. Data from papers

Title	First Author	Year	Field	Int	Mod	Dataset	Data Description	Links	Comment
Bayesian Networks for Clinical Decision Support in Lung Cancer Care	Sesen M. Berkan	2013	cancer	Yes	Yes	NA	LUCADA database	DB	used the Junction Tree algorithm
Lung Cancer Assistant: a hybrid clinical decision support application for lung cancer care.	Sesen M. Berkan	2014	cancer	Yes	Yes	NA	LUCADA database	Soft-ware	based on prev. paper
Modeling interrelationships between health behaviors in overweight breast cancer survivors: Applying Bayesian networks	Xu S	2018	cancer	Yes	NA	Yes	Dataset is not full. 333 postmenopausal overweight or obese breast cancer survivors participating	Dataset	
Impact on place of death in cancer patients: a causal exploration in southern Switzerland	Kern H.	2020	cancer	Yes (?)	Yes	by request	116 adult patients who died from cancer between 2015 and 2016 in southern Switzerland	Soft-ware	

Title	First Author	Year	Field	Int	Mod	Dataset	Data Description	Links	Comment
Prediction of lung cancer incidence on the low-dose computed tomography arm of the National Lung Screening Trial: A dynamic Bayesian network	Petousis P.	2016	cancer	(?)	Yes	by request	National Lung Screening Trial	Models available in supplementary files	Shorter dataset
Quantitative analysis of breast cancer diagnosis using a probabilistic modelling approach	Liu S.	2018	cancer	No	Yes	Yes	Breast Cancer Wisconsin Dataset (UCI)	Dataset	Used two datasets. Second one is not available
Cancer classification from time series microarray data through regulatory Dynamic Bayesian Networks	Kourou K.	2020	cancer	No	No	Yes	GSE14426, GSE37182, GSE5462	?	Pancreatic cancer dataset, colon cancer dataset, breast cancer dataset
Survivability modelling using Bayesian network for patients with first and secondary primary cancers	Wang K	2020	cancer	No	Yes	Partially	National Health Insurance (NHI) database of Taiwan		Resulting conditional probability tables in the paper
Preoperative risk stratification in endometrial cancer (ENDORISK) by a Bayesian network model: A development and validation study	Reijnen, C.	2020	cancer (predict LNM)	No	Yes	by request	International Federation of Gynecology and Obstetrics (FIGO) or ENITEC	Model	Risk interpretation (Bounds) available

Title	First Author	Year	Field	Int	Mod	Dataset	Data Description	Links	Comment
A clinical decision support system learned from data to personalize treatment recommendations towards preventing breast cancer metastasis	Jiang, X.	2020	breast cancer	No	Yes	Yes	LSDB-5YDM	Dataset	
A privacy-preserving Bayesian network model for personalised COVID19 risk assessment and contact tracing.	Fenton, N.	2020	COVID-19	No	Yes	Yes	Data in the model	Age-naRisk model	Made a sensitivity analysis
Application of intelligence-based computational techniques for classification and early differential diagnosis of COVID-19 disease	Akin-nuwesi, B.	2021	COVID-19	No	No	Yes		Soft-ware & data	

Title	First Author	Year	Field	Int	Mod	Dataset	Data Description	Links	Comment
Application of a novel hybrid algorithm of Bayesian network in the study of hyperlipidemia related factors: a cross-sectional study.	Wang, X.	2021	Hyperlipidemia	No	Yes	by request	Hyperlipidemia in Shanxi province; A total of 4567 complete data were left, including 2236 males, accounting for 49.0%, and 2331 females, accounting for 51.0%	R code available in supplementary files	Setted inter.iamb-Tabu hybrid algorithm to establish the BNs structure; Used a Netica software; Bounds available in file sup.1
Application of tabu search-based Bayesian networks in exploring related factors of liver cirrhosis complicated with hepatic encephalopathy and disease identification	Zhang, Z.	2019	cirrhosis of the liver	No	Yes	Yes	Information about patients with cirrhosis who were hospitalized in the Department of Gastroenterology, First Hospital of Shanxi Medical University from January 2006 to December 2015 and who had complete medical records	Data in supplementary files	Used Netica

Title	First Author	Year	Field	Int	Mod	Dataset	Data Description	Links	Comment
A new Bayesian network-based risk stratification model for prediction of short-term and long-term LVAD mortality	Loghmanpour NA	2015	heart failure	Yes	Yes	by request	Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) database	Model in sup.files	GeNie
Predicting the causative pathogen among children with osteomyelitis using Bayesian networks - improving antibiotic selection in clinical practice	Wu Y	2020	osteomyelitis	Yes (?)	Yes	NA	From a retrospective cohort (n=295) of children admitted to Princess Margaret Hospital for Children (PMH), Perth, WA, Australia from 2002 to 2007	Model in sup.files	Netica
A Primer on Bayesian Decision Analysis With an Application to a Kidney Transplant Decision.	Neapolitan R	2016	Kidney Transplant	Yes (?)	Yes	NA		Model in paper	KDRI index for bounds

Title	First Author	Year	Field	Int	Mod	Dataset	Data Description	Links	Comment
Causal inference for violence risk management and decision support in forensic psychiatry	Constantinou, A	2015	psychiatry	Yes	Yes	NA	VoRAMSS dataset The dataset consists of questionnaire, interviewing and assessment data from 386 patients, out of whom 343 are males and 43 are females. Interviews were performed at 6 and 12 months post-discharge	Model in paper	Made a sensitivity analysis
Risk assessment and risk management of violent reoffending among prisoners	Constantinou, A	2015	psychiatry	Yes	Yes	NA	Prisoner Cohort Study (PCS) dataset	DSVM-P model (NA)	Made a sensitivity analysis
Development of a Bayesian network for the risk management of violent prisoners	Coid JW	2016	psychiatry	Yes	Yes	NA	The sample included 953 prisoners (778 men and 175 women) assessed after release into the community.	Model in paper	Used AgenaRisk. Violence risk management with interventions. Compare results with HRC-20, SAPROF, PANSS scales.

Title	First Author	Year	Field	Int	Mod	Dataset	Data Description	Links	Comment
Development of a Bayesian network for risk management of patients discharged from forensic mental health services	Coid JW	2016	psychiatry	Yes	Yes	NA	VoRAMSS dataset; The sample used for parameterisation and learning of the network included 386 patients discharged from MSSs in the UK (343 men, 43 women) over a 12-month period.	Model in paper	Used AgenaRisk. Compare results with HRC-20, SAPROF, PANSS scales.
Analyzing the performance of fuzzy cognitive maps with non-linear hebbian learning algorithm in predicting autistic disorder	Kannappan, A.	2011	autistic disorder	No	No	Yes	In paper	No model	
A Bayesian network decision model for supporting the diagnosis of dementia, Alzheimer's disease and mild cognitive impairment	Seixas, F.	2014	dementia	No	Yes	Paid	Duke University Medical Center (Washington, USA) and the Center for Alzheimer's Disease and Related Disorders	Data	Model in paper
Reducing COPD Readmissions: A Causal Bayesian Network Model	S. Lee	2018	COPD	Yes	Yes	NA	Dataset from St. Mary's Hospital	Model in paper	

Title	First Author	Year	Field	Int	Mod	Dataset	Data Description	Links	Comment
A probabilistic data-driven framework for scoring the preoperative recipient-donor heart transplant survival	Dag A	2016	heart transplant survival	No	No	Yes	UNOS dataset	Data and software available to download	Sensitivity analysis
Predicting graft survival among kidney transplant recipients: A Bayesian decision support model	Topuz, K.	2018	kidney transplant	Yes(?)	No	NA	The UNOS data set included information on all kidney waiting-list registrations and transplants that had been recorded in the U.S and reported between June 30, 2004, and March 31, 2015	Model in paper. United Network for Organ Sharing (UNOS) data	Bounds available. Sensitivity analysis
Analysis for warning factors of type 2 diabetes mellitus complications with Markov blanket based on a Bayesian network model	Liu S.	2020	type 2 diabetes mellitus	No(?)	Yes	by request	dataset was collected from National Health Clinical Center between 1st January 2009 and 31st December 2009	Model in paper Datasets	

Title	First Author	Year	Field	Int	Mod	Dataset	Data Description	Links	Comment
A Dynamic Bayesian Network model for long-term simulation of clinical complications in type 1 diabetes	Marini S.	2015	type 1 diabetes	Yes	Partially	Yes	Diabetes Control and Complications Trial / Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC)	Dataset	
CBN: Constructing a clinical Bayesian network based on data from the electronic medical record	Shen Y.	2018	EHR	No	No	Yes	?	Sql-scenario Software	Used ODDs ratio. Automatically construct a Bayesian topology by K2 algorithm
An ontology-driven clinical decision support system (IDDAP) for infectious disease diagnosis and antibiotic prescription	Shen, Y.	2018	disease diagnosis and antibiotic using	No	No	Yes	OWL file; based on the IDO, NCBI, HPO, DrugBank, and DO databases OWL available.	Software was deleted from git	OWL file structure NA
An intelligent system for prognosis of noncommunicable diseases' risk factors	Pittoli F.	2018	CAD	No	No	Partially	Pima Indians Diabetes Data Set	Model in paper	CAD risk factors and their values intervals.

Title	First Author	Year	Field	Int	Mod	Dataset	Data Description	Links	Comment
From Personal Observations to Recommendation of Tailored Interventions based on Causal Reasoning: a case study of Falls Prevention in Elderly Patients	Chaieb, S.	2022	Falls Prevention in Elderly Patients	Yes	Yes	Yes	1810 elderly patients from the multidisciplinary falls consultations, between January 2005 and December 2018, at Lille University Hospital,	Model in paper	
Urinary tract infections in children: building a causal model-based decision support tool for diagnosis with domain knowledge and prospective data	Ramsay J.	2022	Urinary tract infections	No	Yes	Yes	From May 2019 to November 2020, 391 children were enrolled in the prospective cohort study	Models & data	
Application of a Tabu search-based Bayesian network in identifying factors related to hypertension	Jinhua Pan	2019	Hypertension	No	Yes	Yes	In total, 39 neighborhood committees and villages in Shanxi Province were selected as survey sites	Dataset Model in paper	Used Netica

Table 2. Other datasets

Dataset	Context	Sample size	No. of features	Link
post-op	determine where patients in a postoperative recovery area should be sent to next	90	8	UCI
contraceptive	contraceptive method choice	1473	9	UCI
lymph	lymphography	148	18	UCI
tumor		339	17	UCI
nurs		12960	8	UCI
Medical Insurance dataset	make predictions of the insurance cost people will have to pay	3630	6	Kaggle
lung	lung cancer data set	32	56	UCI
Breast Cancer Prediction	predict from the dataset whether a person has Breast Cancer: Benign or Malignant	683	11	Kaggle
Erbil Heart Disease Dataset	common factors or characteristics contribute to the cardiovascular disease	333	21	Kaggle
Pima Indians Diabetes	Diagnostically predict whether or not a patient has diabetes, based on certain diagnostic measurements included in the dataset	768	9	Kaggle
Coronary Heart Disease	Contains cases of coronary heart disease (CHD) and variables associated with the patient's condition	462	10	Kaggle
Haberman's Survival	Survival of patients who had undergone surgery for breast cancer	306	4	Kaggle
Breast Cancer Wisconsin	Predict whether the cancer is benign or malignant	569	32	Kaggle

Table 3. Databases

Database	Description	Link
WorldBank	Data catalog	link
OptumLabs Data Warehouse	160 million de-identified records across claims and clinical information to conduct investigations on populations	link
NSCH Datasets	National Survey of Children’s Health	link
NLST Datasets	Cancer Institute	link
Medical Information Mart for Intensive Care	Freely available medical data for research	link
Osteosarcoma Database	Contains 911 protein-coding genes and 81 microRNAs associated with osteosarcoma	link
Hospital Episode Statistics (HES)	Containing details of all admissions, outpatient appointments and A and E attendances at NHS hospitals in England	link
MIMIC-III Clinical Database	Health-related data associated with over forty thousand patients who stayed in critical care units of the Beth Israel Deaconess Medical Center between 2001 and 2012	link
CENTER-TBI	Contains prospectively collected data of more than 4,500 patients with TBI in Europe	link
ISCoS	Spinal Interventions and Surgical Procedures Basic Data Set	link
BioGPS	Gene and protein function	link
GDC portal	Genomic Data Commons Data Portal	link
PPMI	Parkinson’s disease	link
Open Data UK	data published by central government, local authorities and public bodies	link
National Lung Screening Trial	Lung Cancer	link
STS Intermacs Database	North American registry for the clinical outcomes of patients who receive an FDA-approved mechanical circulatory support (MCS) device to treat advanced heart failure	link
BayesFusion	Interactive Model Repository. Models available to download	link

Section C

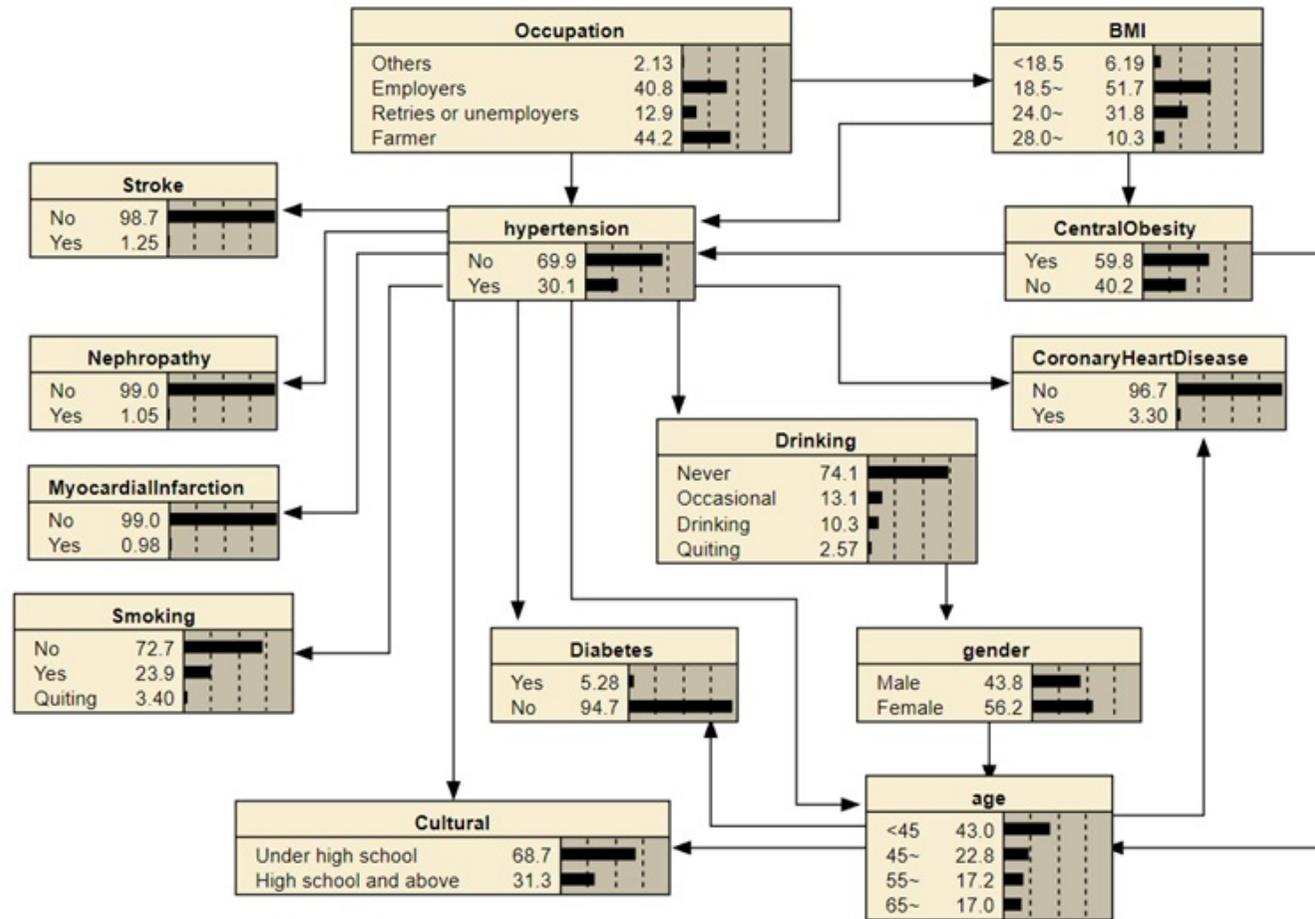


Fig. C1: Application of a Tabu search-based Bayesian network in identifying factors related to hypertension

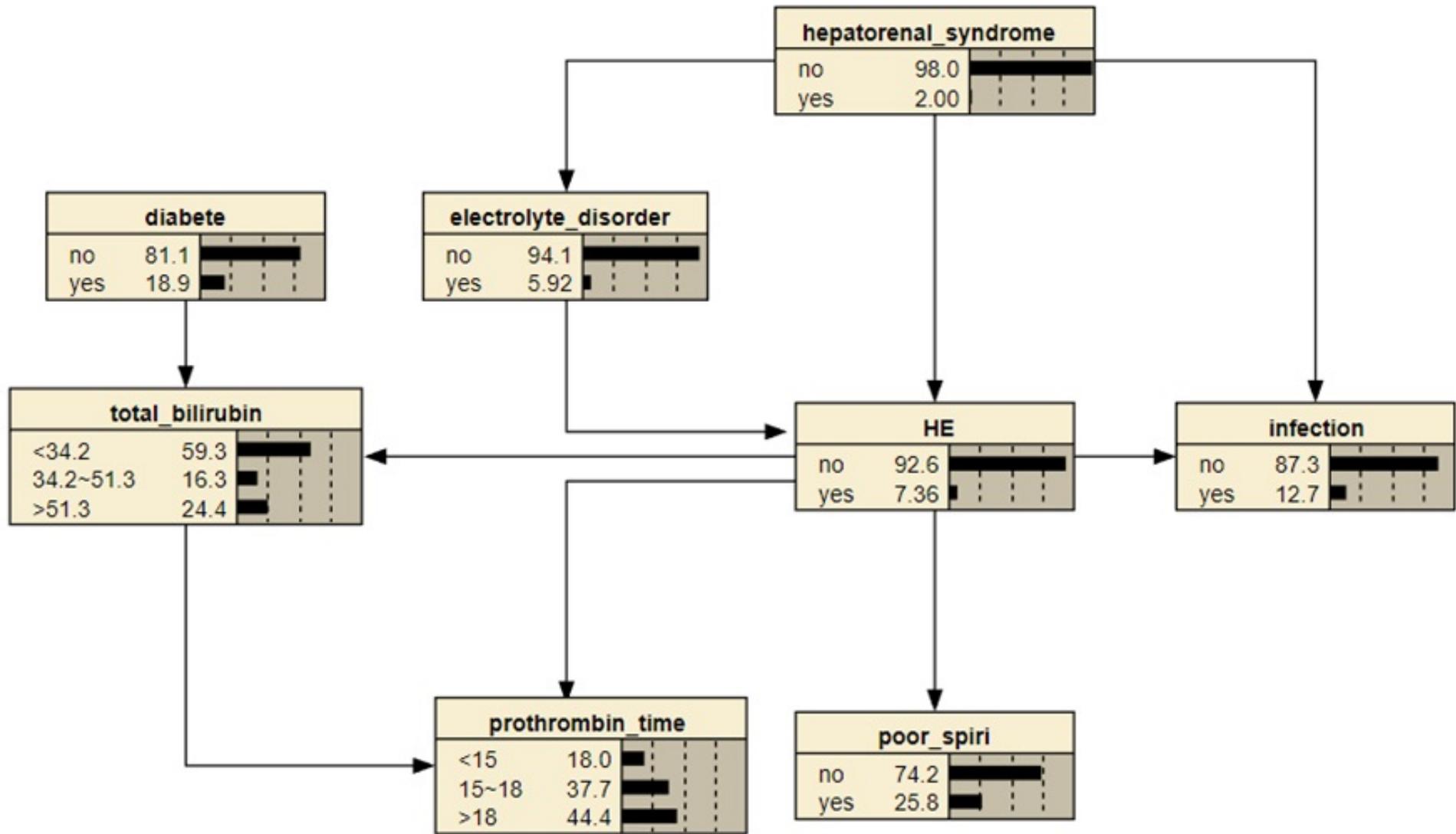


Fig. C2: From Application of tabu search based Bayesian networks in exploring related factors of liver cirrhosis complicated with hepatic encephalopathy and disease identification

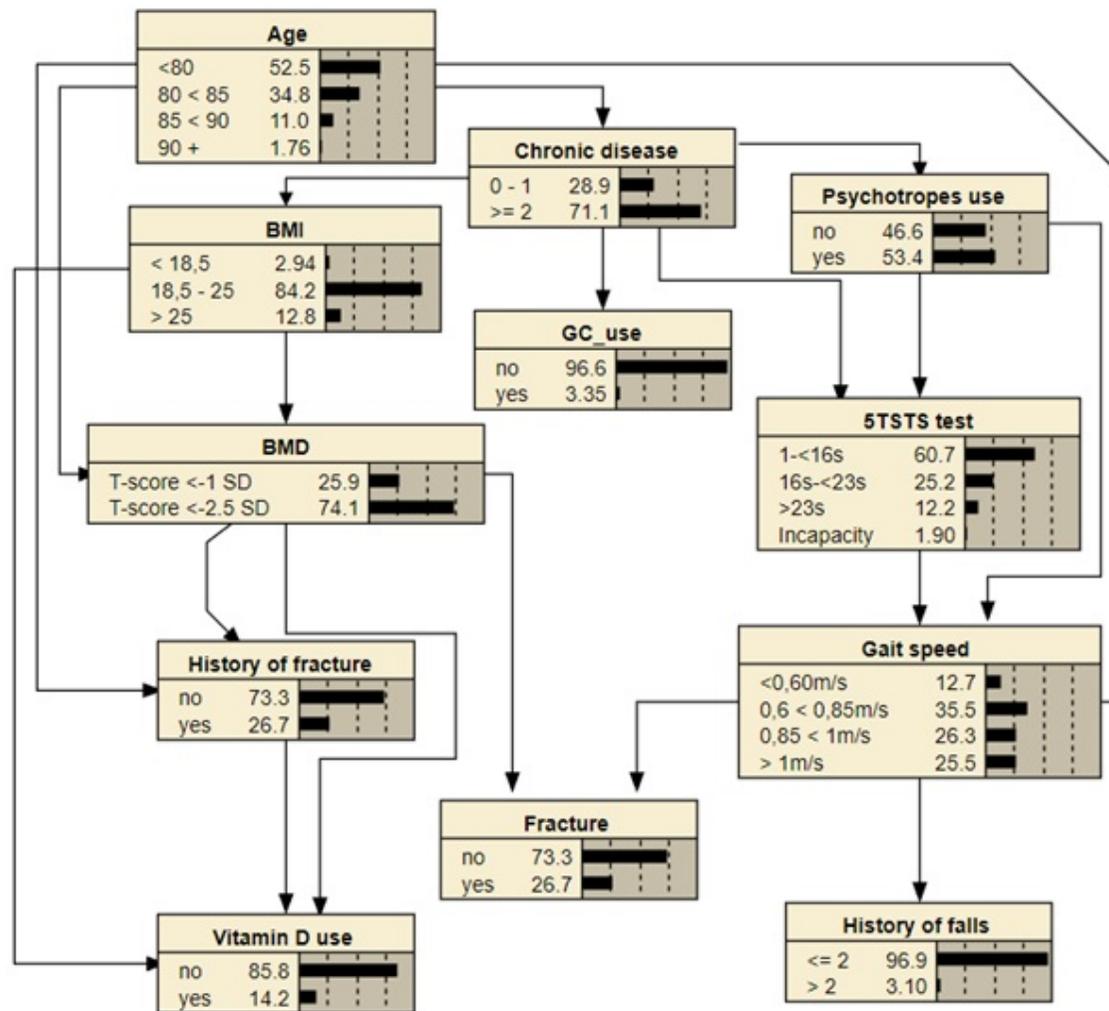


Fig. C3: From Hip Fracture in the Elderly A Re-Analysis of the EPIDOS Study with Causal Bayesian Networks

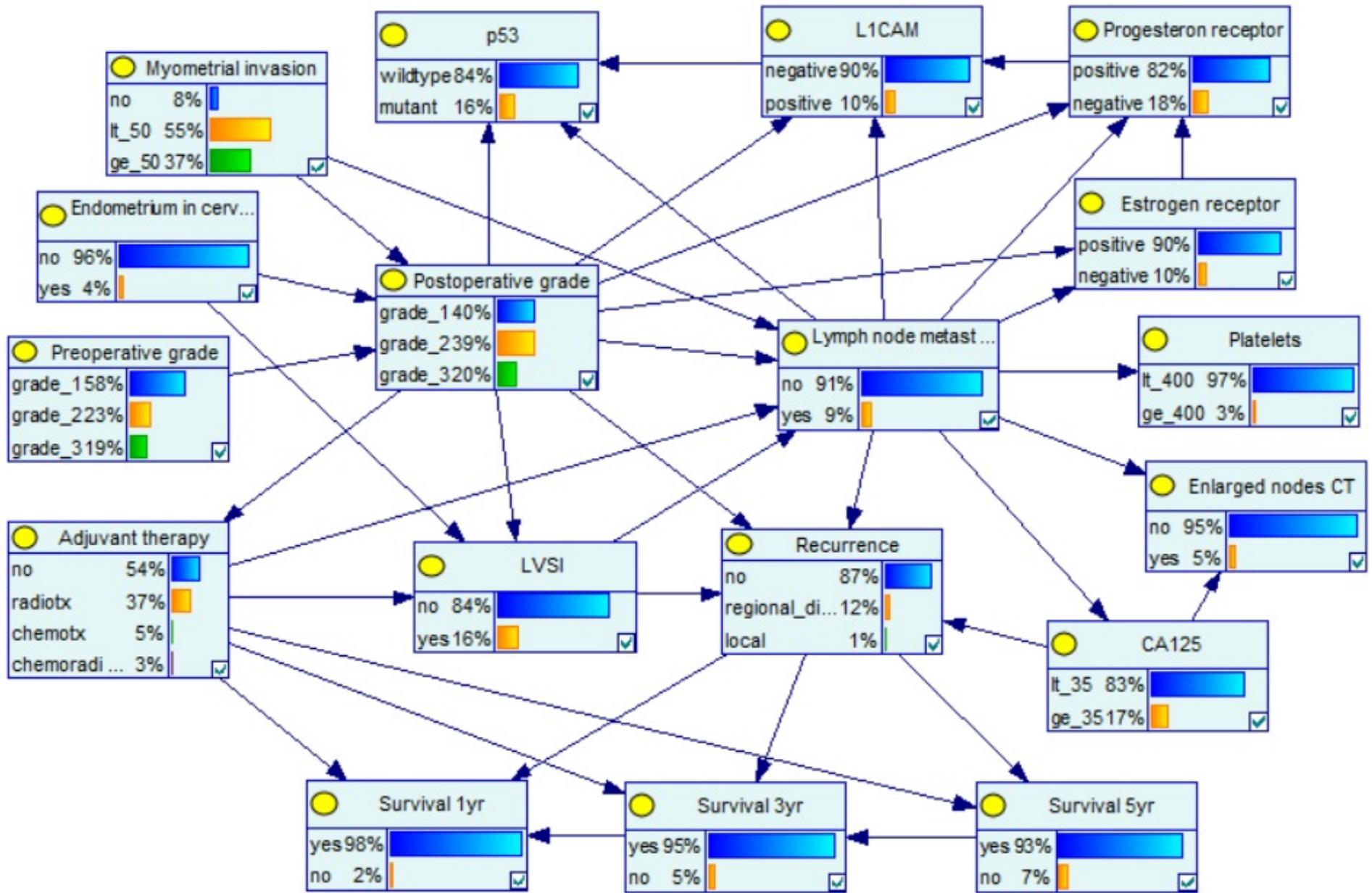


Fig. C4: From Preoperative risk stratification in endometrial cancer (ENDORISK) by a Bayesian network model: A development and validation study

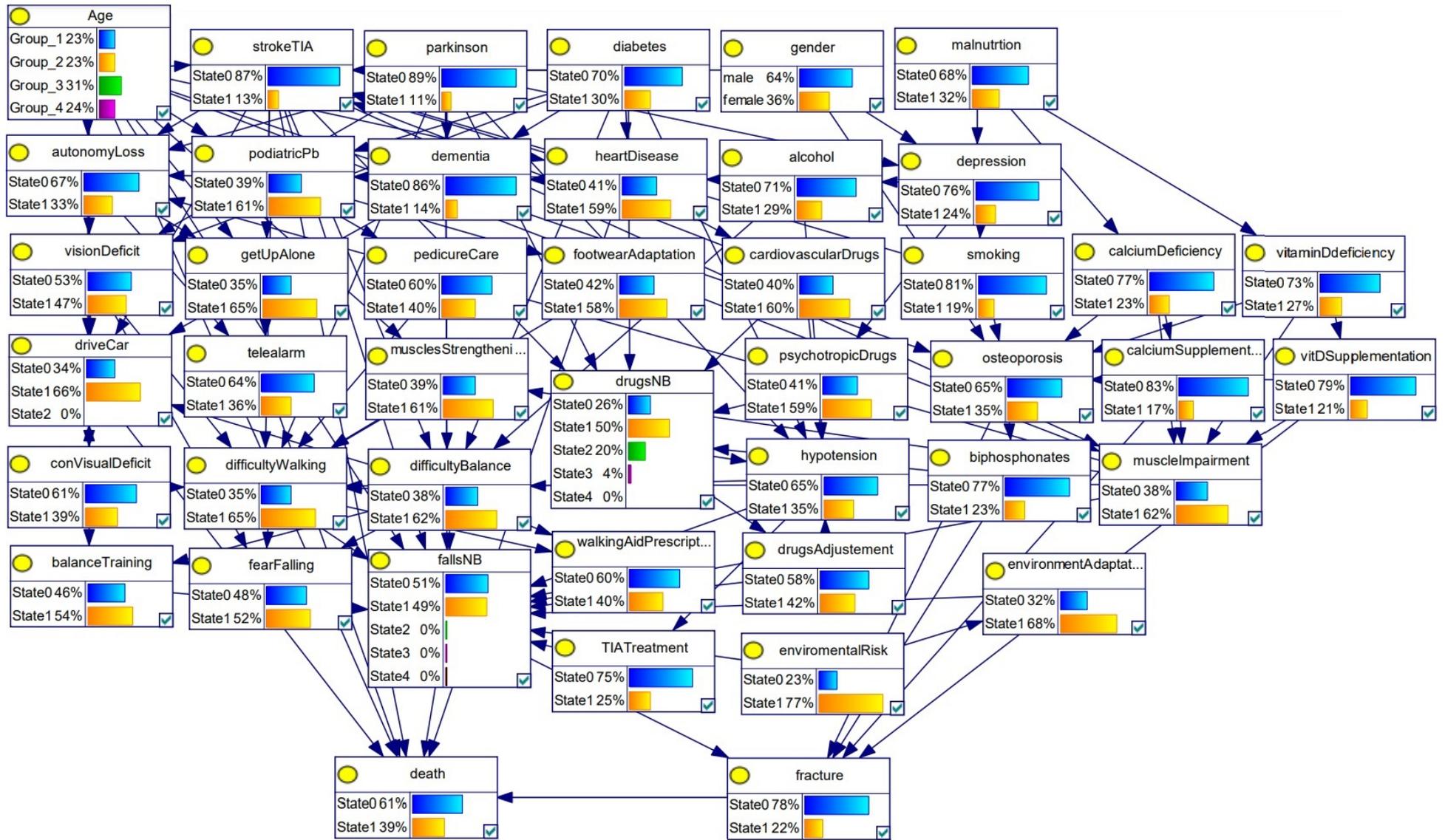


Fig. C5: Paper "From Personal Observations to Recommendation of Tailored Interventions based on Causal Reasoning: a case study of Falls Prevention in Elderly Patients" (A proposed network for interventions)

Appendix D

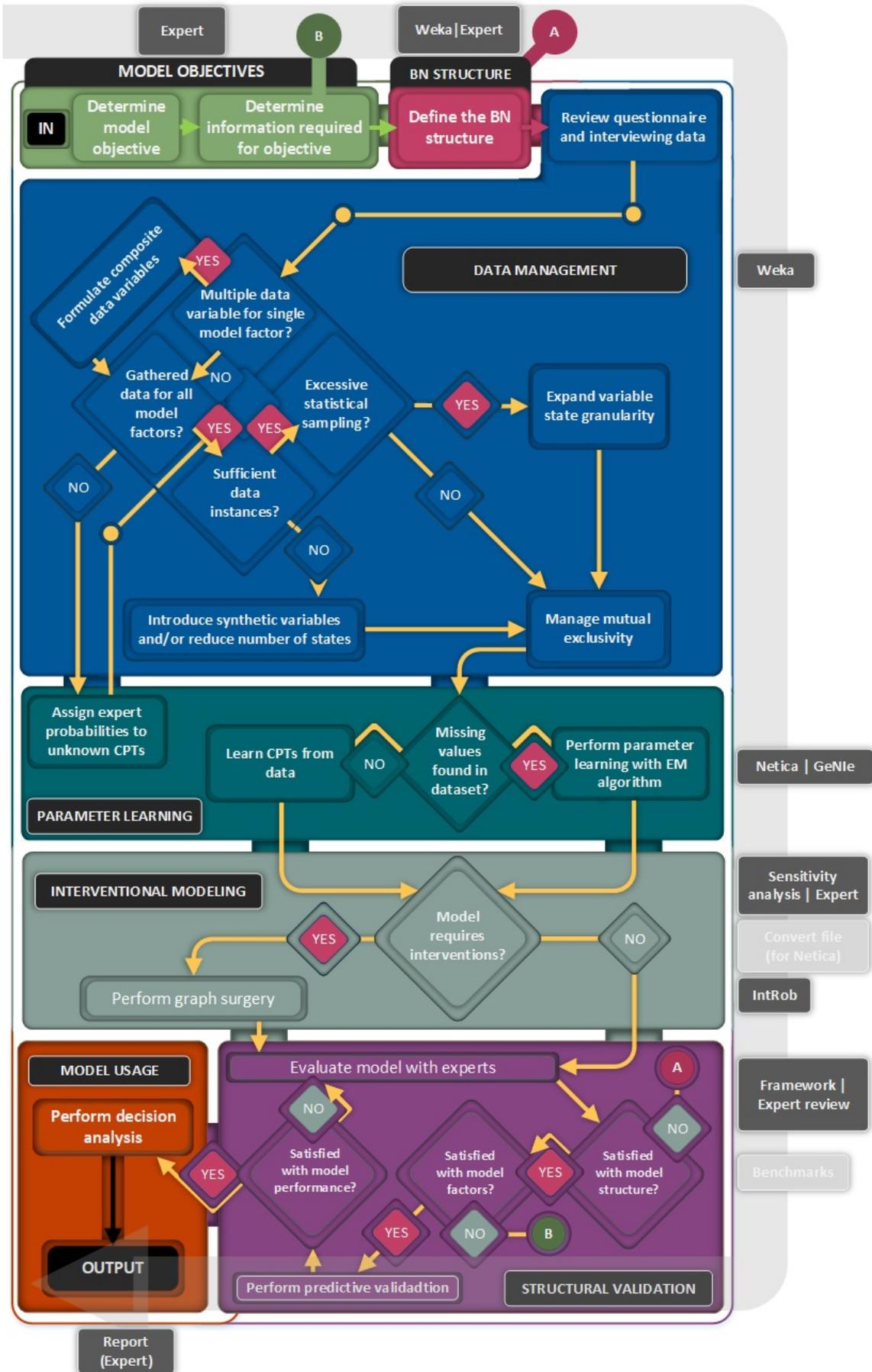


Fig.D1: Framework

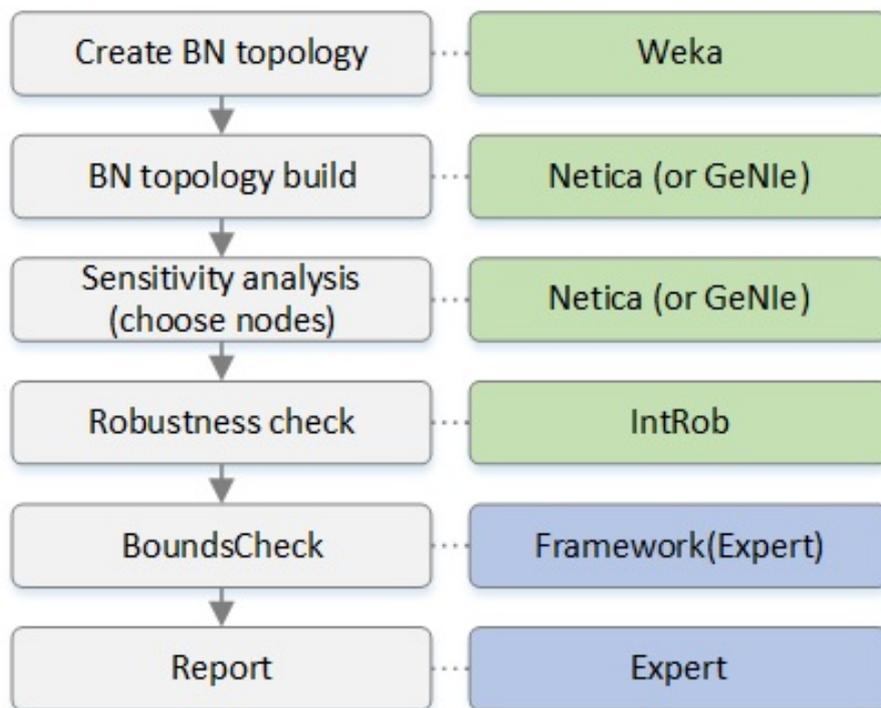


Fig.D2: simplify