

wiseR: Helping your decisions from complex datasets

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wiseR is an interactive, end-to-end Bayesian Network Analysis and publishing platform for learning cross-validated structure, inferences, topology, visualization in interventional and observational data. It is powered by R, Shinydashboard, bnlearn and visNetwork packages.

Getting Started

To install latest developmental version of wiseR in R

```
devtools::install_github('SAFE-ICU/wiseR')
```

To launch the app:

```
wiseR::wiser()
```

Bayesian Networks

Why Bayesian Networks?

Networks are one of the most intuitive representations of complex data. However, most networks rely on pair-wise associations which limits their use in making decisions. Bayesian Networks (BNs) are a class of probabilistic graphical models which can provide quantitative insights from data. These can be used both for probabilistic reasoning and causal inference depending upon the study design.

A BN is a directed acyclic graph and provides a single joint-multivariate fit on the data with a list of conditional independencies defining the model structure. Unlike multiple pair-wise measures of association, fitting a model decreases the chance of false edges because the structure has to agree with global and local distributions. Importantly, unlike most other forms of Artificial Intelligence and Machine Learning, BNs are not a black-box model. These are transparent, interpretable and help the user in reasoning about the data generative process by looking at the motifs. This can be immensely useful in learning systems such as healthcare where a feedback between the clinicians and the learning system is paramount for adoption. The structure (independencies) of a BN can be learnt directly from data using machine learning or be specified by the user, thus allowing expert knowledge to be injected. After the dependence structure within the data is learnt (or specified) the parameters are learnt on the network using one of many possible approaches. wiseR provides most of the existing approaches such as constraint based algorithms and score-based algorithms for parametrization of the Bayesian Network. Recommendations as per the state-of-the-art in the literature are specified at each step of the BN learning process (i.e. the recommendation of score based algorithms over constraint based algorithms for learning structure and Bayesian Information Criteria over Akaike Information Criteria for evaluating the fit). Parametrization of the network enables predictions and inferences. These inferences can be purely observational ("seeing" the state of a variable and its effect on neighbours) or causal ("doing" something to a variable, i.e. interventions and observing the effect on downstream nodes). wiseR provides scoring methods both for observational (e.g. Bayesian Information Criterion) and interventional (e.g. modified Bayesian Dirichlet Equivalent score) datasets.

The flexibility provided by BNs in probabilistic reasoning and causal inference has made these one of the most widely used artificial intelligence methods in Computer Science. However, the sophistication required to code all the features has limited their use by domain experts outside of computer science, e.g. clinicians. wiseR plugs this gap by creating a GUI for the domain experts and is an end-to-end solution for learning, decision making and deploying decision tools as dashboards, all from the wiseR platform.

What do the motifs (junctions) reveal about the data-generating process

Carefully learnt BNs are representations of the generative process that produced the data. These generative processes are captured in the form of three basic motifs present in the network: chain, fork and collider junctions.

Chain (Mediator effect)

This motif is the simplest structure in a BN with a sequence of nodes pointing in the same direction. The intermediate nodes are called mediators and conditioning on any of the mediators makes the flanking nodes independent of each other. A mediator can be thought of as a mechanism, hence capturing the information about mechanism removes the need for capturing the triggering process, hence making the triggering process independent of the outcome.

Fork (Confounders effect)

The second type of structure observed in a BN is a common parent pointing towards two or more child nodes. The parent represents the common cause and not accounting for the parent is a common source of error (confounding) in many statistical models built upon real world data. A folk example of such an effect is Age as a confounder (common cause) of IQ and shoe-size in children. Failure to condition upon age will lead to a spurious correlation between the IQ and shoe-size and change our reasoning (hence predictions) about the system being modeled.

Collider or a V-structure (Inter-causal reasoning)

These are one of the most interesting motifs in an Bayesian Network and are indicated by two nodes pointing towards a single child node. Although the two parent nodes are not causally connected, conditioning on the state of the common child opens up a ghost-path for probabilistic inference flow (inter-causal reasoning) which can explain many intriguing paradoxes (e.g. the Monty Hall problem).

Walkthrough of wiseR functionalities

Pipeline

The logical flow of analysis and reasoning conducted with **wiseR** is shown in Figure S1.

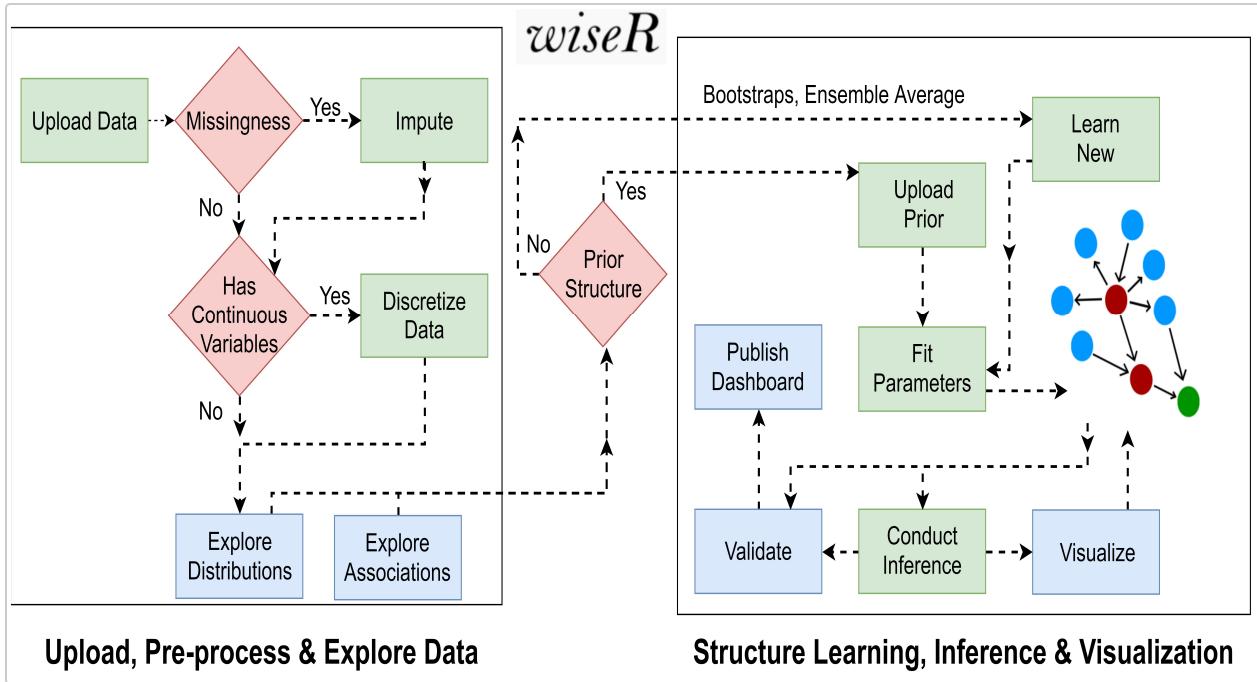


Figure S1. Flowchart showing logic of *wiseR*

Start

Calling the `wiseR()` function from the **wiseR** package launches the application in the default browser. The recommended browser for **wiseR** is Chrome. On launching the application for the first time, it conducts background checks, which takes 5-10 seconds depending upon the machine. This delay only happens on the first launch and all subsequent launches take less than a couple of seconds to initialize the user interface.

The toolbar on the left side of the page has icons for navigating to home, analysis engine, github development version and team information at any point of time.

Click “Start Analyzing” for navigating to the analysis engine with tabs specifying the functions. Hovering over most of the tabs brings up a tool-tip that briefly describes the function performed on that action.

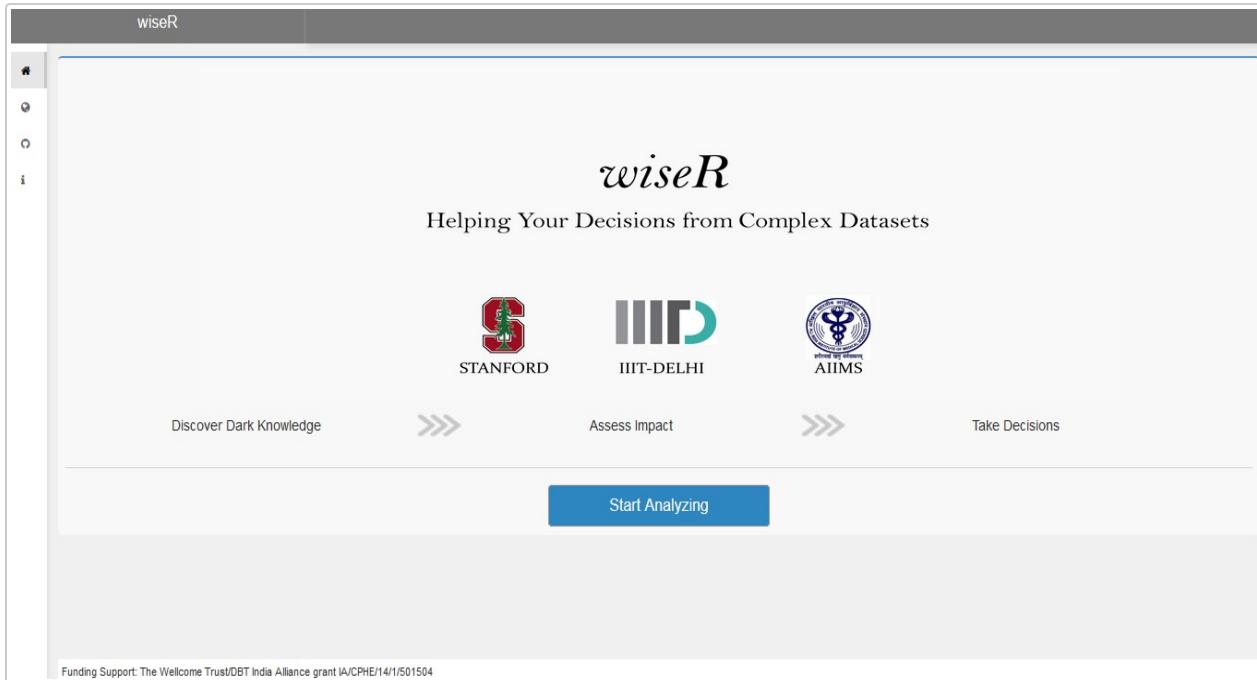


Figure S2. Homepage of the *wiseR* application

Main page of the *wiseR* engine

“Start Analyzing” takes us to the main page of the ***wiseR*** engine. An intuitive left-to-right ordering of tabs guides the user into the analysis. This page has 5 tabs named ‘App Settings’, ‘Data’, ‘Association Network’, ‘Bayesian Network’ and ‘Publish your dashboard’, each tab covering a specific functionality (Figure S3). Each of these is described next.

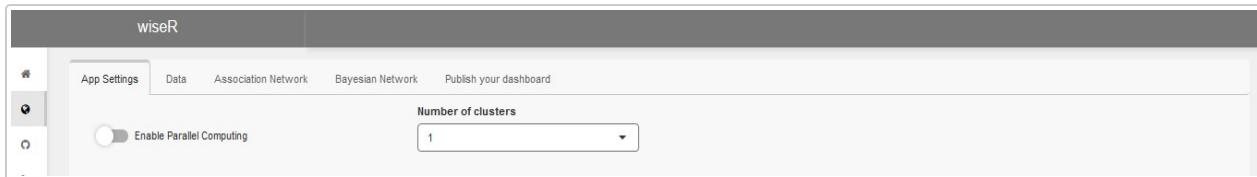


Figure S3. Functional tabs on the main page of the *wiser* engine and the first tab (App Settings) for parallel computation.

App Settings

This tab (Figure S3) is used to set the parallel computing option (number of cores) for learning BN structure. Learning structure is known to be NP-hard problem and may be time consuming on large datasets. Setting the number of clusters allows each core to learn a structure when bootstrap learning is performed. Since learning one structure cannot be parallelized, this is an example of task parallelization.

Data

This tab is used to load, pre-process and explore the dataset (Figure S4.)

The dataset panel contains the upload and preprocess menu while explore panel is used to visualize the distribution of the data.

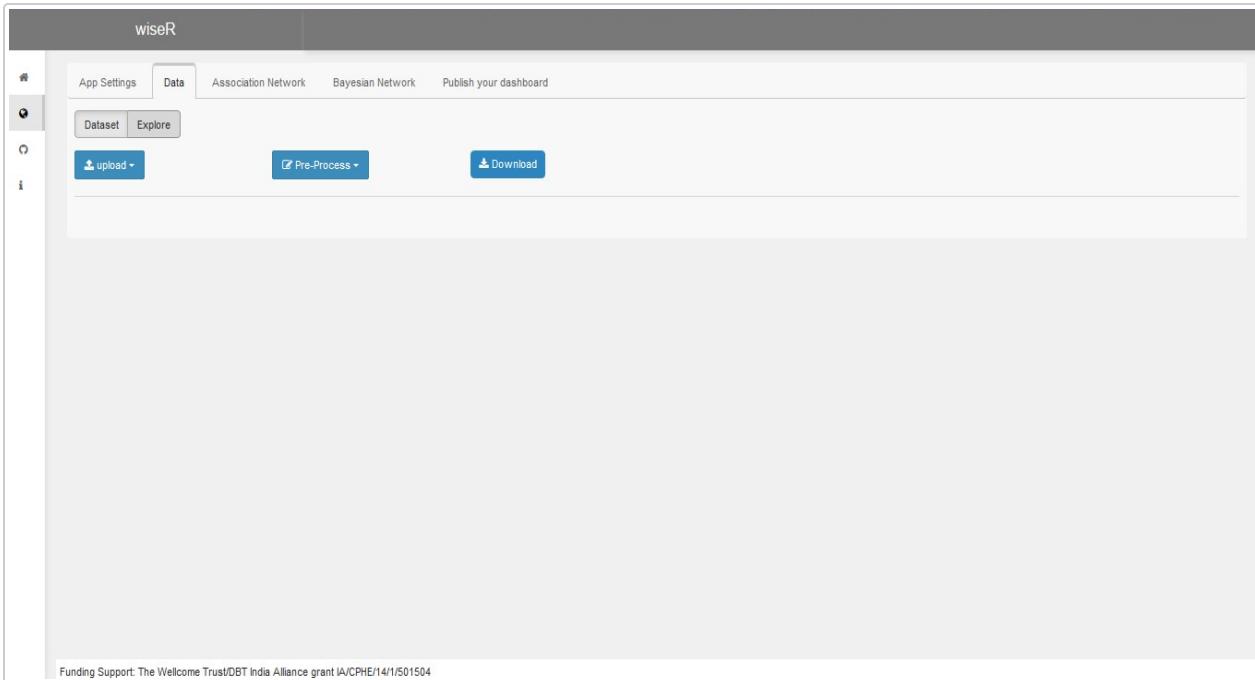


Figure S4. Data upload, exploration and pre-processing functions.

Upload

Users can upload their own data in one of the '.CSV', '.RData' & '.txt' formats. For large data, saving the data as .RData is recommended for its compression of data, hence efficient storage. For '.txt' files different options of file formatting are provided such as:

- Comma Separated
- Semi-colon Separated
- Tab separated
- Space Separated

Users trying the app can work with the pre-loaded datasets (Alarm, Hailfinder, Asia, Coronary) to replicate BN analysis commonly demonstrated with these datasets.

Users must note that the default setting of the app is to treat all variables with less than 53 levels as factor variables. Variables with more than 53 levels are treated as numeric variables and the user is prompted for discretization of such numeric variables to factors. While this is a convenient general option, it may be true that a numeric variable may have less than 53 levels in a particular dataset. In such cases, the user can un-check this option and specify the numeric variables explicitly to be converted to factors in the next step.

Current limit of file upload is 8000 mb, however it is recommended to use .RData for large datasets.

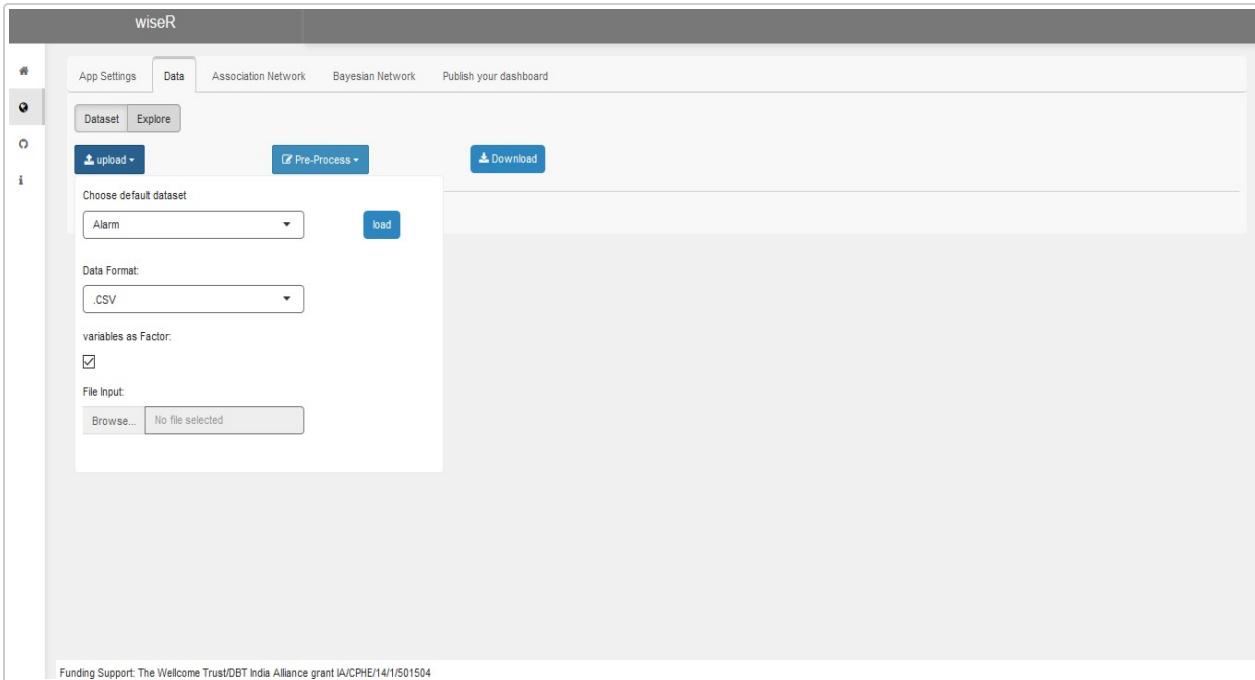


Figure S5. Features of the upload subsection

Pre-process

The preprocess menu is used to edit the data before using through the app. It is essential that data is discrete and complete for learning association network and bayesian network. Multiple options to pre-process the data have been provided.

- User can convert any variable which has been misclassified as numeric to factor
- User can convert any variable which has been misclassified as factor to numeric
- User can choose from a number of algorithms to discretize their data - Hybrid(Recommended), Hartemink (Recommended), K-means, Quantile, Frequency, Interval
- Hartemink requires 2 parameters 'break' and 'ibreak' which can be passed using the text input boxes.
- user can also transpose their data frame, which is especially useful in case of gene expression data
- User is also given the option to sort the columns of data alphabetically
- User can also select unnecessary variables and delete them from the data using the delete button. A rest button is also provided to undo the delete operations in case of mistakes.
- Option for adjusting the learning for interventional data is also provided. User can simply select the variable which holds the interventional classification and adjust the learning to it.

Figure S6. Features of the pre-process subsection

Download

This button is provided in case the user wants to download the dataset in current state as a .CSV file

	CVP	PCWP	HIST	TPR	BP	CO	HRBP	HREK	HRSA	PAP	SAO2	FIO2	PRSS	ECO2	MINV	MVS	HYP	LVF	APL	ANES	PMB	INT
1	NORMAL	NORMAL	FALSE	LOW	NORMAL	HIGH	HIGH	HIGH	HIGH	NORMAL	NORMAL	LOW	HIGH	ZERO	HIGH	NORMAL	FALSE	FALSE	FALSE	FALSE	FALSE	NOR
2	NORMAL	NORMAL	FALSE	NORMAL	LOW	LOW	HIGH	HIGH	HIGH	NORMAL	LOW	NORMAL	HIGH	ZERO	ZERO	NORMAL	FALSE	FALSE	FALSE	FALSE	FALSE	NOR
3	NORMAL	HIGH	FALSE	NORMAL	NORMAL	HIGH	HIGH	HIGH	HIGH	NORMAL	LOW	NORMAL	NORMAL	ZERO	ZERO	NORMAL	FALSE	FALSE	FALSE	FALSE	FALSE	NOR
4	NORMAL	NORMAL	FALSE	LOW	LOW	HIGH	HIGH	HIGH	HIGH	NORMAL	NORMAL	NORMAL	HIGH	ZERO	ZERO	NORMAL	FALSE	FALSE	FALSE	FALSE	FALSE	NOR
5	NORMAL	NORMAL	FALSE	LOW	LOW	NORMAL	HIGH	HIGH	HIGH	NORMAL	LOW	NORMAL	LOW	ZERO	ZERO	NORMAL	FALSE	FALSE	FALSE	FALSE	FALSE	NOR
6	NORMAL	NORMAL	FALSE	LOW	NORMAL	HIGH	HIGH	HIGH	HIGH	NORMAL	LOW	NORMAL	HIGH	HIGH	ZERO	NORMAL	FALSE	FALSE	FALSE	TRUE	FALSE	NOR
7	NORMAL	NORMAL	FALSE	LOW	LOW	HIGH	HIGH	HIGH	HIGH	NORMAL	LOW	LOW	LOW	ZERO	ZERO	NORMAL	FALSE	FALSE	FALSE	FALSE	FALSE	NOR
8	NORMAL	NORMAL	FALSE	NORMAL	LOW	LOW	HIGH	NORMAL	NORMAL	LOW	LOW	NORMAL	HIGH	ZERO	ZERO	NORMAL	FALSE	FALSE	FALSE	FALSE	FALSE	NOR
9	NORMAL	LOW	FALSE	LOW	LOW	HIGH	HIGH	HIGH	HIGH	NORMAL	LOW	NORMAL	HIGH	ZERO	ZERO	NORMAL	FALSE	FALSE	FALSE	FALSE	FALSE	NOR
10	NORMAL	NORMAL	FALSE	NORMAL	NORMAL	HIGH	HIGH	HIGH	HIGH	LOW	LOW	NORMAL	HIGH	LOW	ZERO	NORMAL	FALSE	FALSE	FALSE	FALSE	FALSE	ESO

Showing 1 to 10 of 20,000 entries

Previous 1 2 3 4 5 ... 2000 Next

Funding Support: The Wellcome Trust/DBT India Alliance grant IA/CPHE/14/1/501504

Figure S7. Button to download dataset

Explore

This section is provided to visualize the distribution of the variables in the dataset. Once the data has been pre-processes(Discretized and complete), the user can select a variable and visualize the plot of its factor distribution.

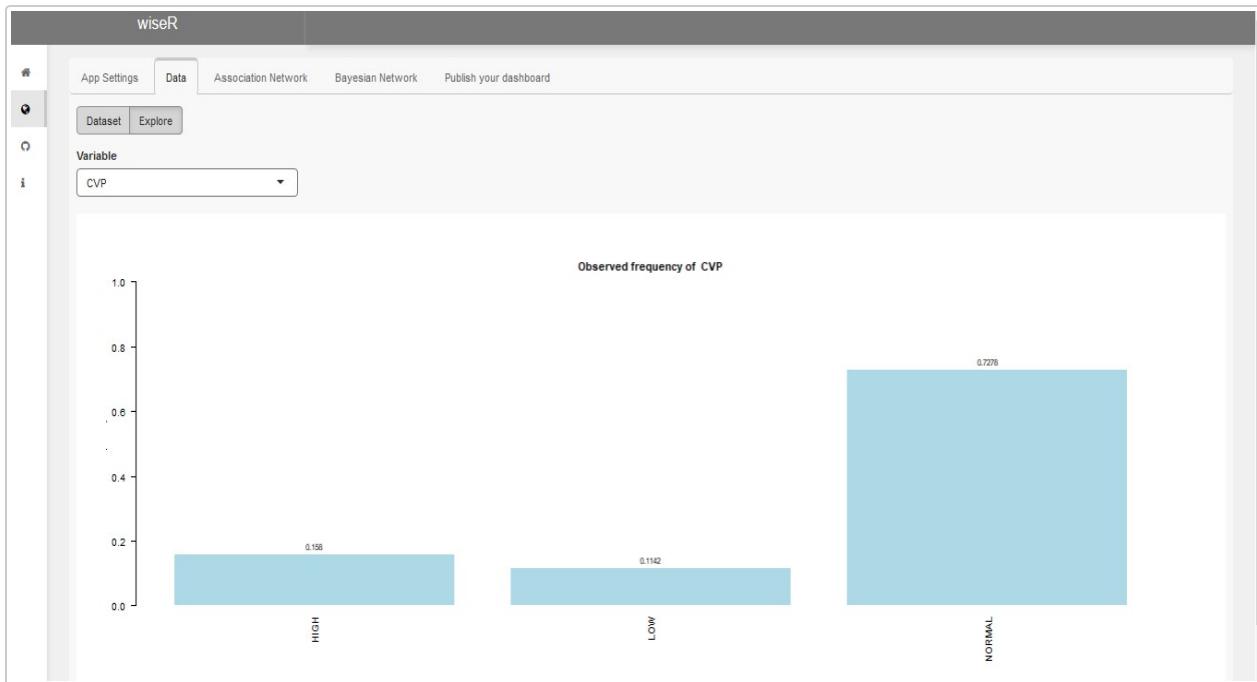


Figure S8. Explore subsection of the databab to visualize distrubutions

Association Network

Even though not directly related association networks are an essential part of bayesian learning. Bayesian networks are often large and complex, which makes the difficult to understand. Learning association networks on the data before bayesian learning can give useful insights from the simplistic structure produced and provides a more targeted approach to bayesian learning.

The app provides multiple options to build and explore association networks.

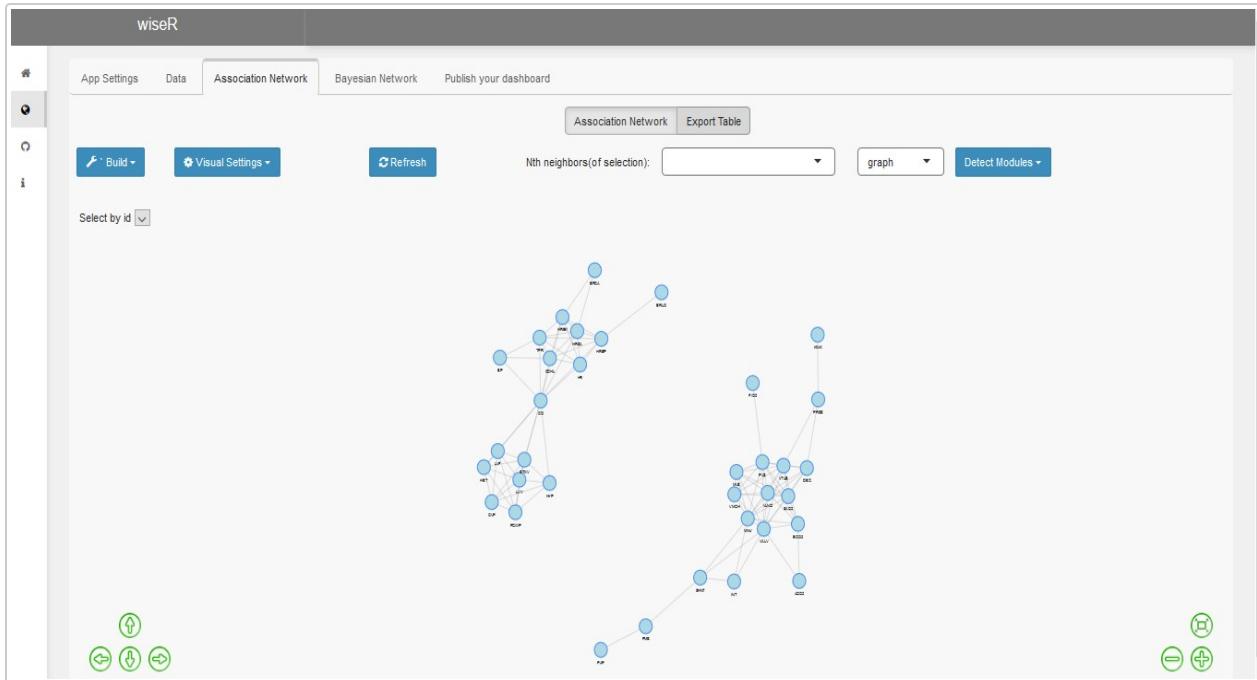


Figure S9. Build and Explore Association networks

Build

The build menu is used to build association networks. It consists of different metrics for association strength which are used to build association networks like

- cramer's V(Recommended)
 - cohen's D
 - Goodman kruskal lambda
 - Tschuprow's T

Each method returns a value between 0 and 1. 0 being two variables are not associated and 1 being highly associated. A threshold value between 0 and 1 can then be set to choose the edges that remain in the association graph based on strength of association.

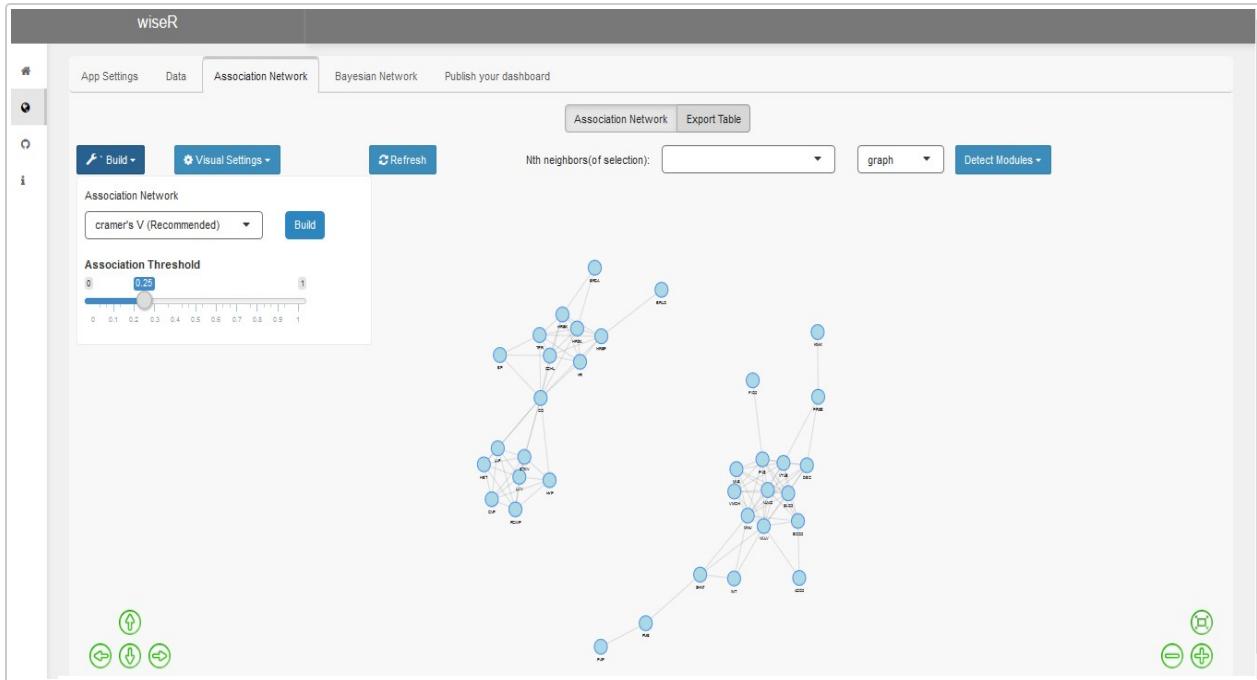


Figure S10. Options to build association networks

Detect Modules

Often large graphs are difficult to explore and contain redundant information. To enable a clutter less analysis feature for module/community detection is provided which highlights different important groups of subgraphs in the original graph. These graphs can be individually explored and analysed.

There are different clustering algorithms available in the app for module/community detection which is powered by linkcomm package, like ward.D (Recommended),ward.D2,single,complete,average,mcquitty, median,centroid for user to choose from.

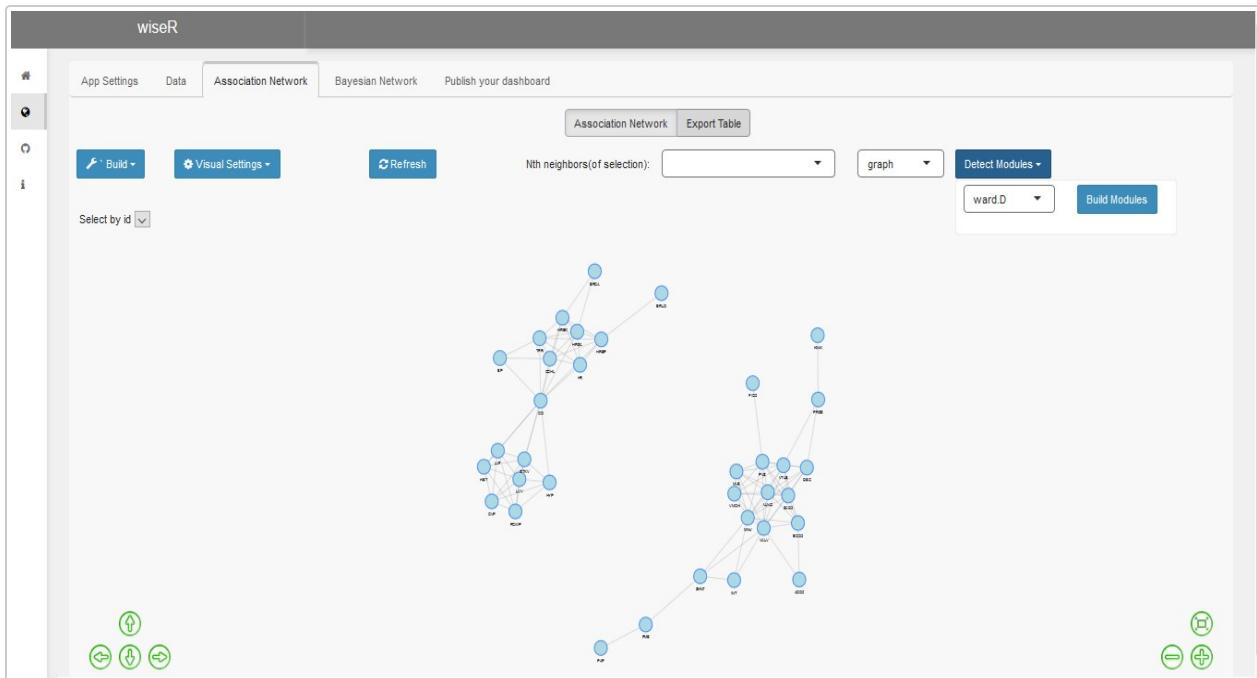


Figure S11. Module detection on association networks

Visual settings

The visual settings menu is used to exploit the graph for better exploration. It comes equipped with many features like variable grouping, which enables the user to group different nodes, by selecting variable names/vector of variable indices/variables belonging to a module and selecting a node shape they want to give these variables.

To ease the exploration of large graphs a threshold for visible neighbor chain is provided, such that clicking on a node only display its neighbors upto that degree.

Another neighborhood variable exploration mechanism is setting value for nth order neighbors, such that clicking on a variable return a list of nth degree neighbors.

User has the option to arrange the graph nodes using different graph layouts. Depending on the graph different layout setups enable ease of exploration. Some useful layouts include mds, tree, sugiyama

User can adjust the font size of the node labels to improve visibility

User also has the option to download the network graph in its current state using the save network option present in the bottom right corner of the graph.

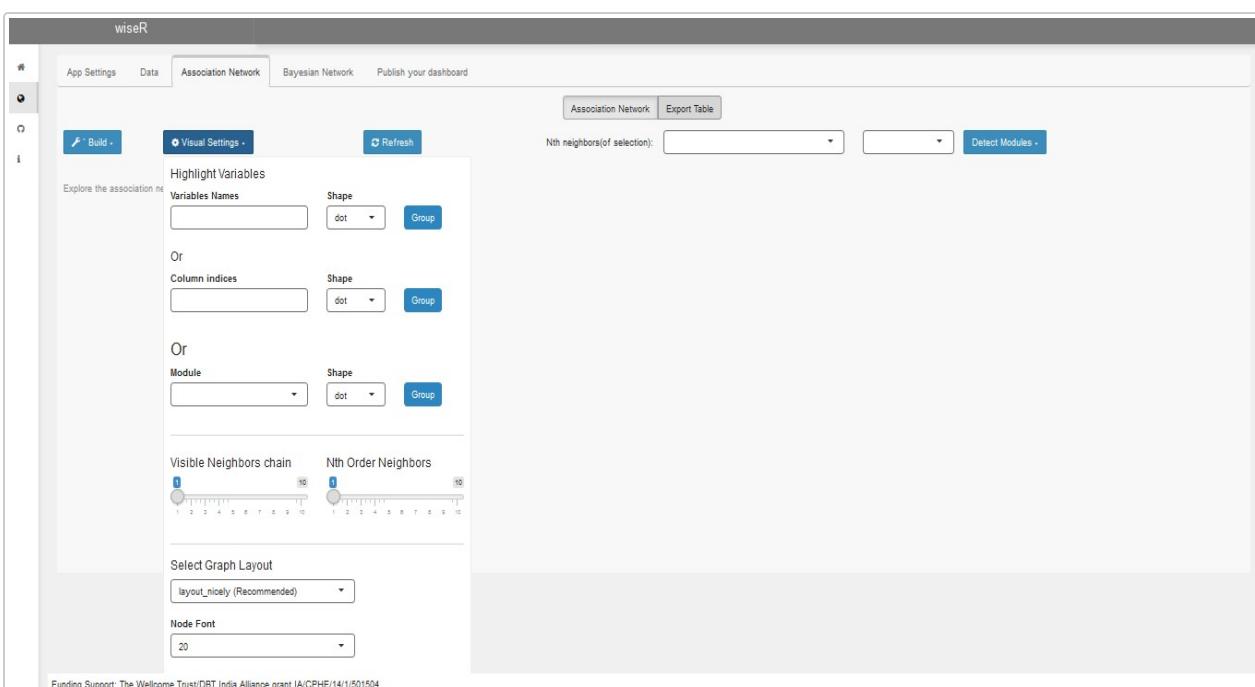


Figure S12. Visual settings to explore association graphs

Export tables

This section is used to visualize the association network produced in a tabular form and also to download it as a .CSV file if needed.

V1	V2	Strength of Association
CVP	PCWP	0.70775327999036
CVP	HIST	0.484717924689875
CVP	HYP	0.633729145847987
CVP	LVF	0.573093174365814
CVP	LVV	0.600319168434443
CVP	STKV	0.254359145232881
PCWP	HIST	0.488416395232902
PCWP	HYP	0.761583090373247
PCWP	LVF	0.58212075842292
PCWP	LVV	0.885148132124862

Showing 1 to 10 of 104 entries

Previous 1 2 3 4 5 ... 11 Next

Funding Support: The Wellcome Trust/DBT India Alliance grant IA/CPHE/14/1/501504

Figure S13. Export the association graph

Bayesian Network

Multiple features have been clubbed into the bayesian learning component of the app to make it as useful as possible. This component of the app is powered by the bnlearn package and tries to cover all the innovative and efficient methods for structure learning as explained in the book.

Nth Neighbors(of selection):

Modules: Detect Modules

Visual Settings

Refresh

Construct bayesian network for taking decisions

Funding Support: The Wellcome Trust/DBT India Alliance grant IA/CPHE/14/1/501504

Figure S14. Build and Explore Bayesian Networks

Structure learning

The structure learning menu incorporates all the need for bayesian learning and has been divided into 5 sections based on use.

Initialize structure

This section enables the user to upload a network graph as a .CSV file to initialize the bayesian learning graph. The section also provides the user the option to add, remove or reverse the direction of any arc, once the graph has been uploaded. (Only used in score-based learning)

The screenshot shows the wiseR app interface with the 'Structure Learning' tab selected. The main area displays a table of edges with columns 'from' and 'to'. A dropdown menu allows users to 'Add' new edges, 'Remove' existing ones, or 'Reverse' their direction. The table currently lists four edges: CVP to PCWP, CVP to TPR, CVP to CO, and CVP to HRBP. Below the table, a note indicates 'Showing 1 to 4 of 4 entries'. At the bottom left, there is a note about funding support from the Wellcome Trust/DBT India Alliance grant IA/CPHE/14/1/501504.

Figure S15. graph initialization settings

Learn Structure

This section is used to learn new bayesian structure through the app.

The user can choose from a number of bayesian learning algorithms such as

- Score-based (Recommended):- Hill Climbing, Tabu
- Constraint-based:- Grow-Shrink, Incremental Association, Fast IAMB, Inter IAMB,PC
- Hybrid Learning:- Max-Min Hill Climbing, 2-phase Restricted Maximization
- Local Discovery:- Max-Min Parents and Children,Semi-Interleaved HITON-PC, ARACNE, Chow-Liu

and can also adjust other bayesian learning parameters such as:

- Parameter fitting algorithm:- Bayesian parameter estimation, maximum likelihood parameter estimation
- Network score:- Bayesian Information Criterion,Bayesian Dirichlet Equivalent,modified Bayesian Dirichlet Equivalent,log-likelihood,Akaike Information Criterion,Bayesian Dirichlet Sparse,Locally Averaged Bayesian Dirichlet (Only used in score-based learning)
- Imaginary sample size (Only used in score-based learning)
- Blacklist(explicitly restrict edges in structure learning) and whitelist(explicitly enforce edges in structure learning) edges by uploading a .CSV file for the same
- Disabling data resampling in bootstrap learning. This is particularly useful for data with very less no. of samples, such that resampling may lead to information loss. This method is only possible for score based algorithms as it requires random graph initialization.

- Bootstrap iterations:- No. of bootstrap iteration to run in case user decided to opt for bootstrapped structure learning
- Bootstrap sample size:- Proportion of data to be used as sample for bootstrap learning
- Edge strength:- Set a threshold value between 0 and 1 to remove edges below that strength from the final structure. Edge strength is basically the probability of occurrence of an edge in each iteration of bootstrap learning
- Edge direction:- set threshold value between 0 and 1 to remove edges below that direction confidence from the final structure. Edge direction is basically the confidence of direction of a learned arc in bootstrap learning.

The user can simple choose the do direct learning or do a bootstrapped one(in which case bootstrap parameters will be used) for more robust structure learning.

Once structure has been learned, parameters such as parameter fitting algorithm and edge strength and direction threshold(For bootstrap learning) can be adjusted without having to re learn the structure through parameter tuning option.

User can also save the learned structure as a bnlearn object in .RData format through the save option.

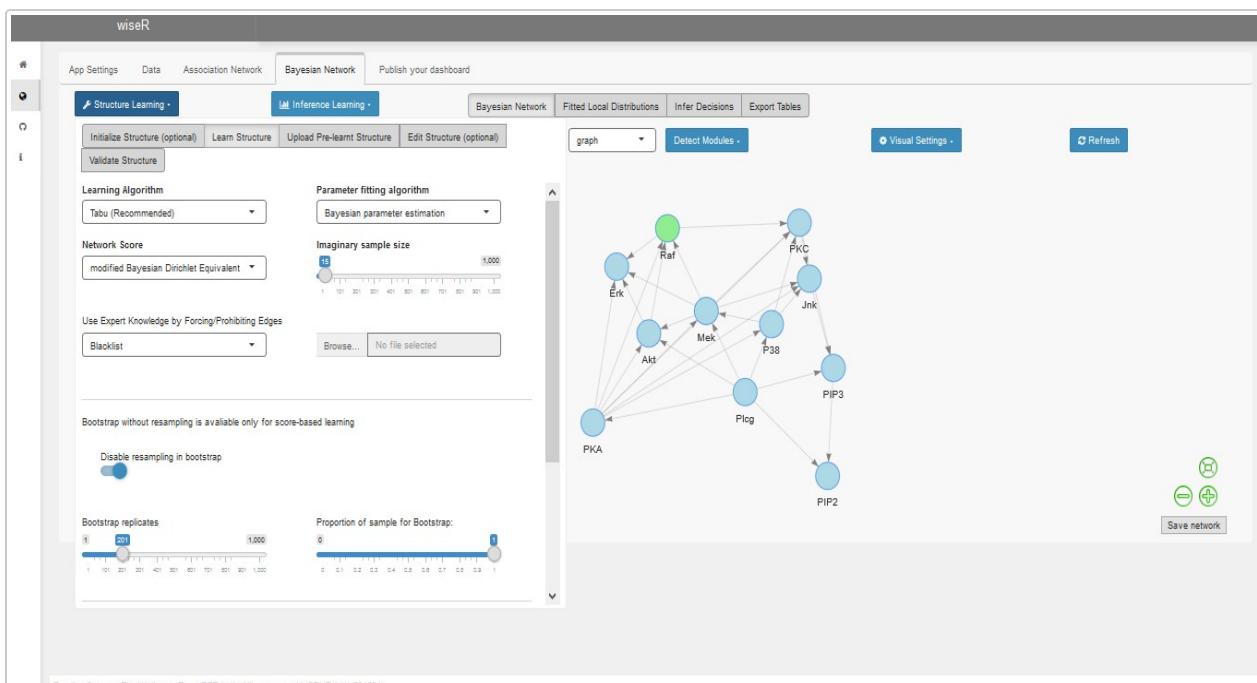


Figure S16. Structure learning settings

Upload pre-learnt structure

This section enables the user to upload an already bayesian structure to be explore through the app. This save the user hassle of learning the structure again and again. The upload structure has to be a bnlearn object uploaded as a .RData file.

User has option to upload both simple and bootstrap structure and adjust there parameters accordingly

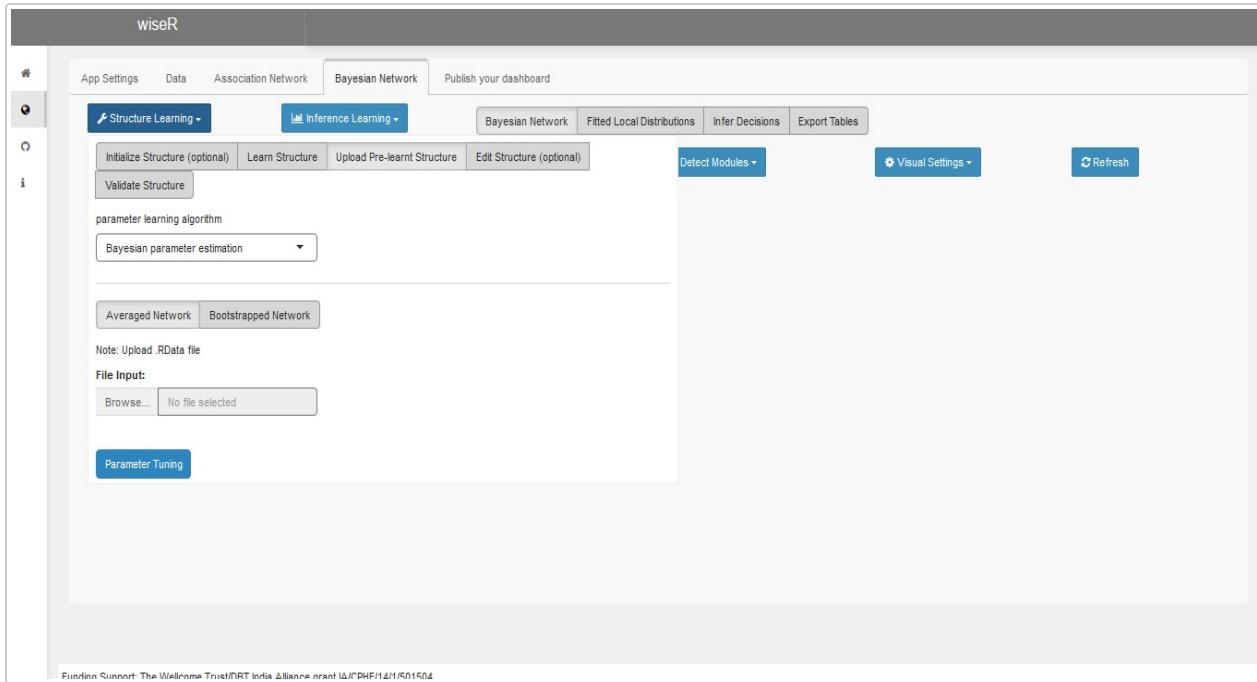


Figure S17. Upload pre-learnt structure

Edit structure

This section enables the user to edit the structure after learning to incorporate additional expert knowledge. User can add new arcs to the structure and remove, reverse the existing ones.

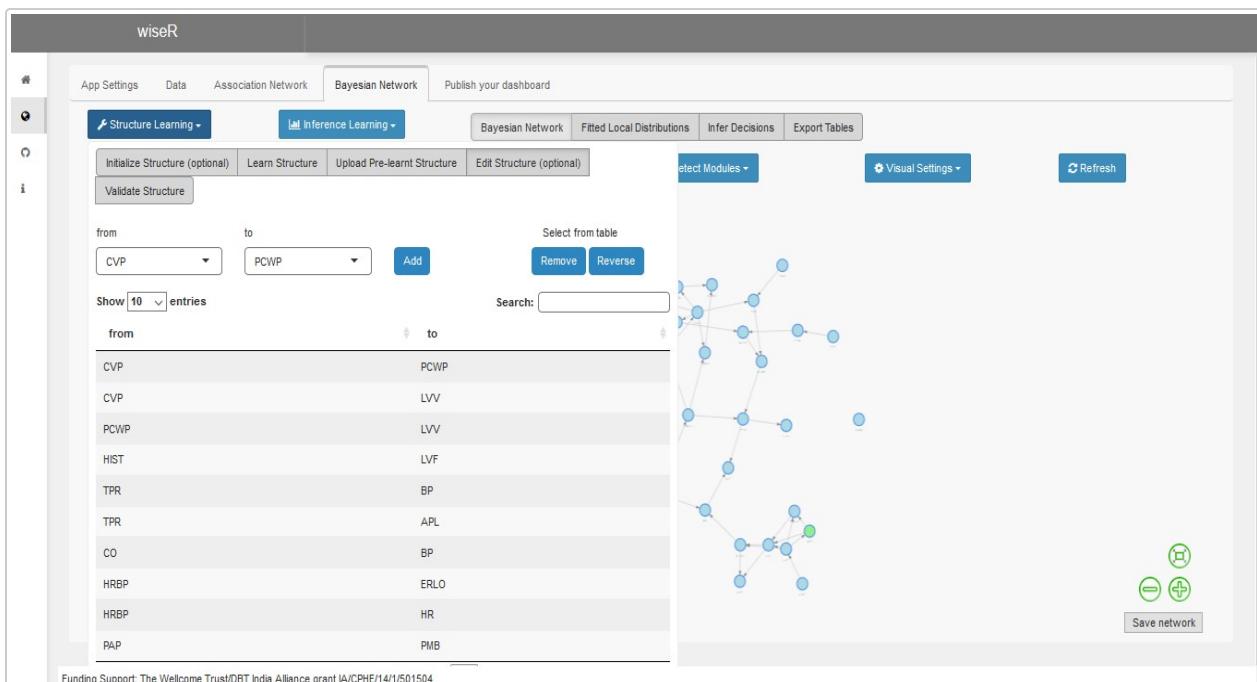


Figure S18. Edit learned structure

Validate structure

This section enable user the option to validate the learned structure, and check the accuracy of the network. User can choose various parameters such as

- Parameter fitting algorithm
- Network score
- Loss function
- Validation algorithm:- 10-fold, Hold-out

to validate the network. The log-likelihood loss and network score outputs produced can then be used to judge the usability of the learned structure.

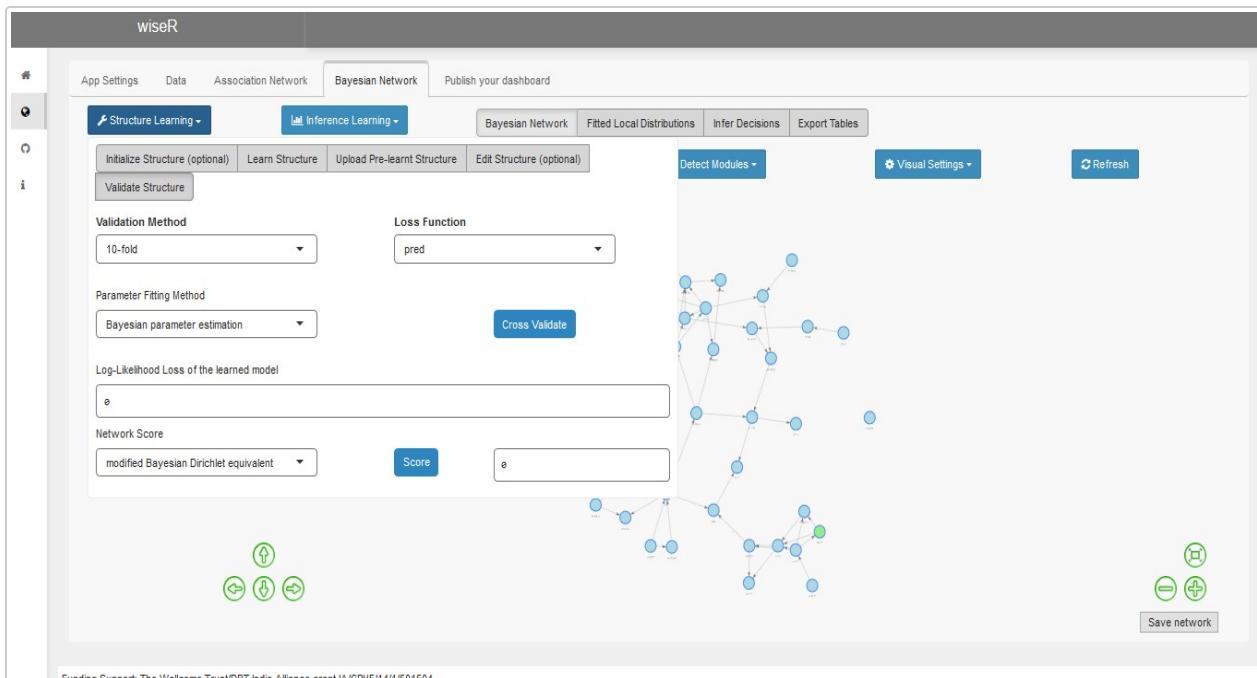


Figure S6. Validate learned structure

Inference Learning

The inference learning menu enables the user to learn and explore conditional probability plots on the learned structure. The user can set an event and multiple evidences can be inserted and removed as per need. This crucial feature enables the user to explore probability plots on event nodes in the network conditionalized on chain of evidences, which is the essence of decision making through bayesian networks.

The app provides 2 means for inference learning

- Approximate (Very fast but sampling based inference, thus varying results on each iteration leading to slightly less accurate probability plots)
- Exact inference (Fast for small networks, slow for large networks but accurate results on each iteration)

While the app learns approximate learning as default, user must explicitly learn exact inferences whenever the structure is learned or updated. The user can than enable exact inferences instead of approximate.

To compensate for wavering accuracy of approximate inference while retaining its speed, option for inference with error bars is given. User can provide the no. of iterations for error plot (Recommended 25). It is observed that the inference plots produced using approximate inference with error bars, is almost as accurate as exact inference, without the time constraint of exact inferences on large networks.

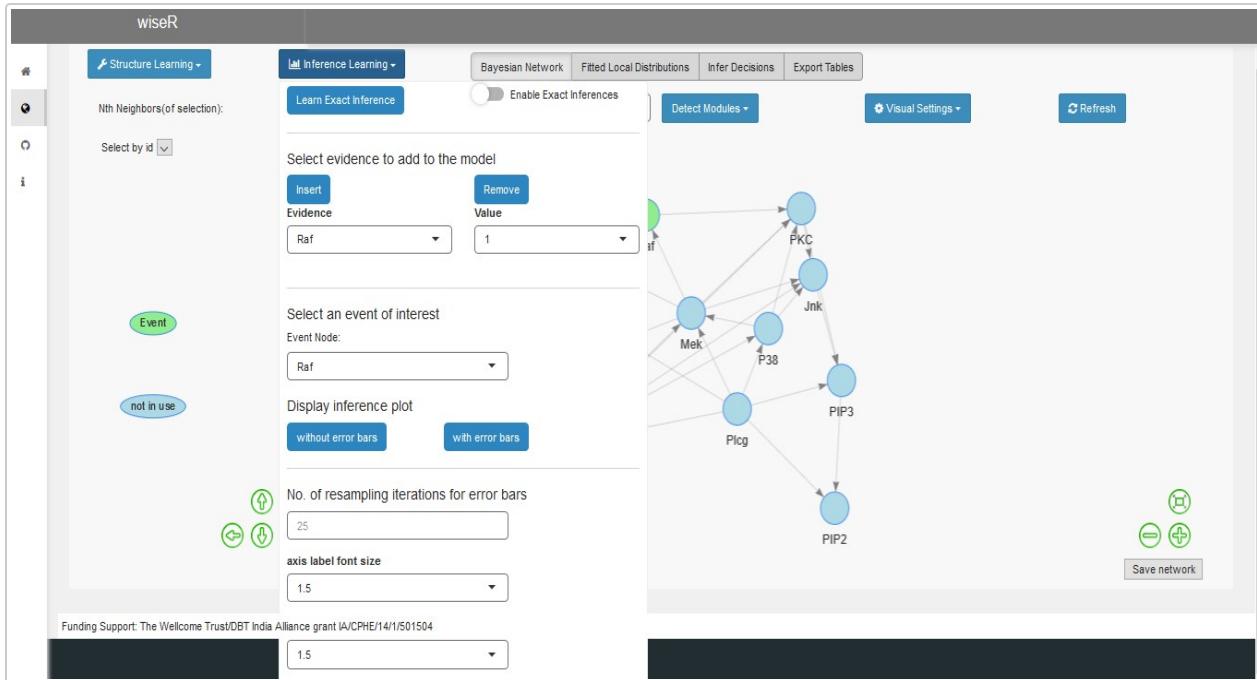


Figure S20. learn and make inferences

Apart from structure learning and inference learning the bayesian network tab is divided into 4 sections for visualization and exploration

- Bayesian network panel is used to explore the learned structure and is equipped with all the graph exploration features as available in association graph

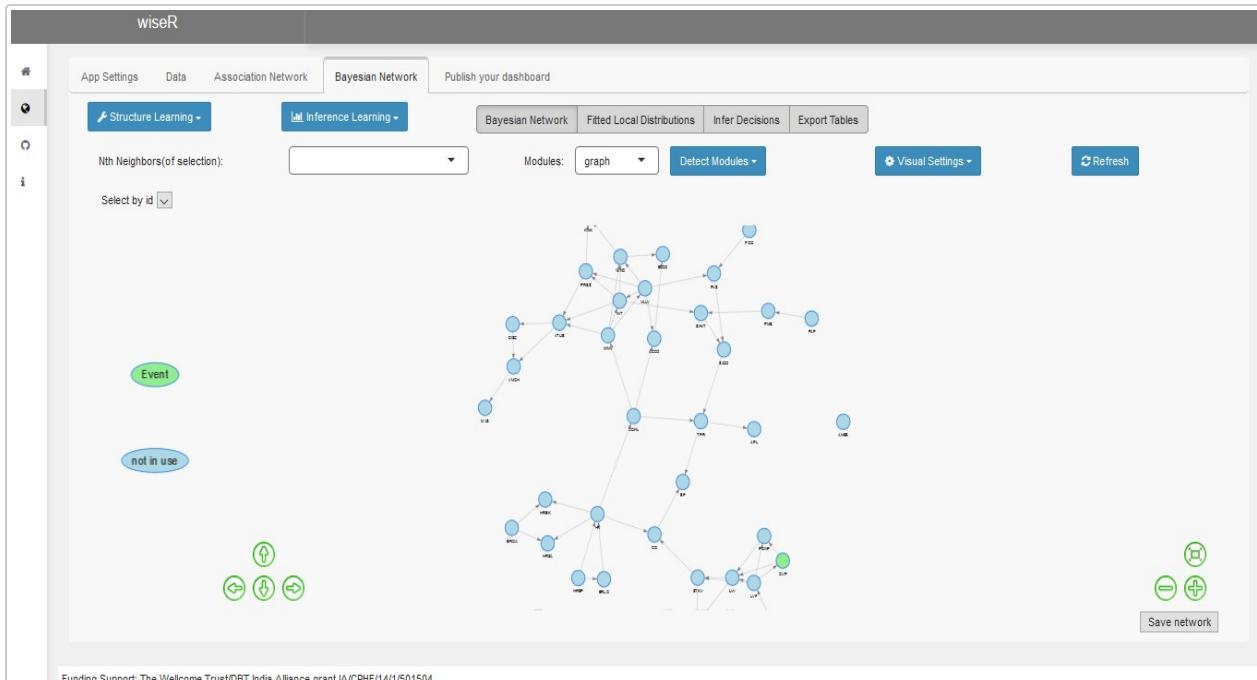


Figure S21. learned bayesian graph

- Fitted local distribution panel is used to explore the local probability distribution tables of variables in the learned network structure

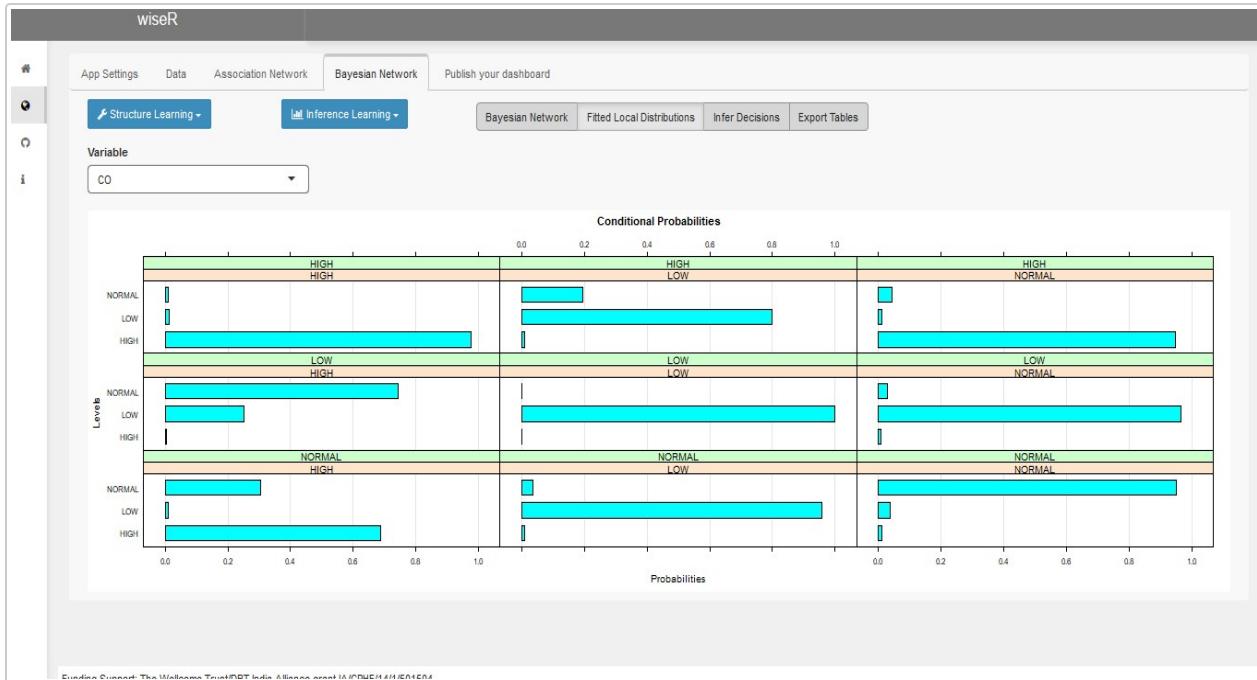


Figure S22. Local probability distribution tables

- Infer decisions is used to visualize the inference plots once the user has chosen the event and evidence nodes. It also has option to sort the plot axis and prune the no. of plot bars

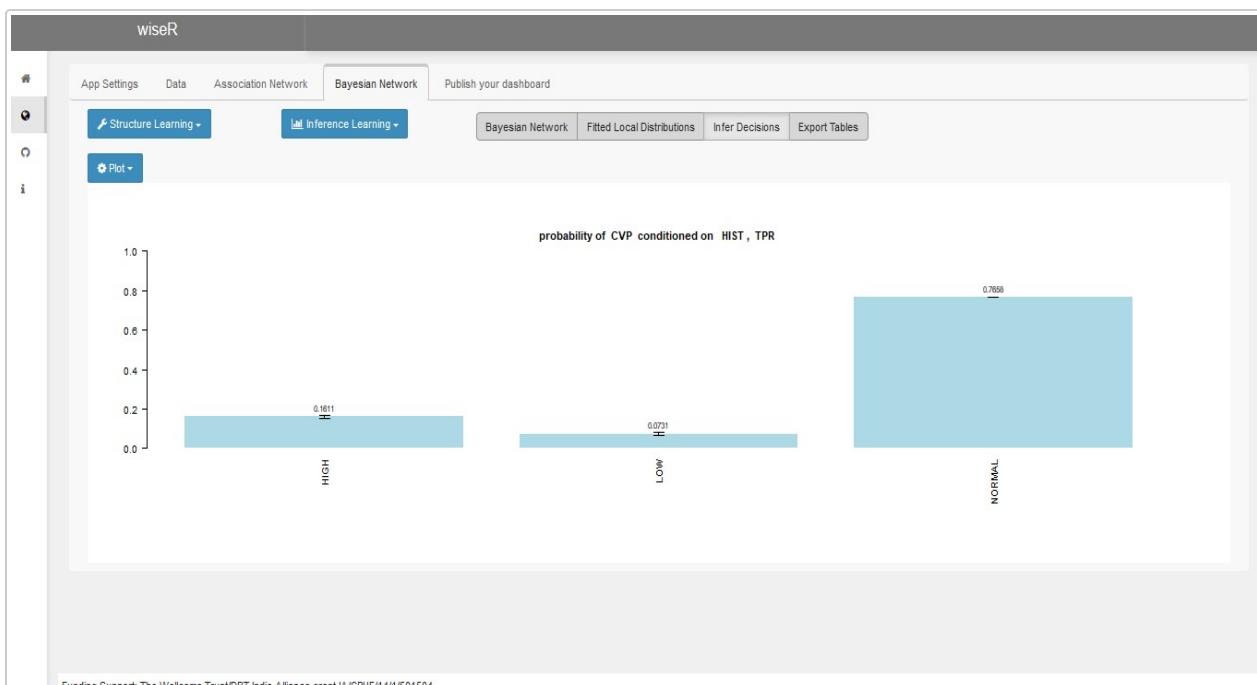


Figure S23. Inference plot

- Export tables section is used to visualize the network graph, blacklist-whitelist edges and variable wise validation results in tabular format. User can also download these tables as .CSV file

The screenshot shows the wiseR app interface. At the top, there's a navigation bar with tabs: App Settings, Data, Association Network, Bayesian Network (which is highlighted in blue), and Publish your dashboard. Below the navigation bar, there are two main sections: Structure Learning and Inference Learning. Under Structure Learning, there's a dropdown menu set to 'Bayesian Graph'. There's also a 'Download' button. On the right side of the interface, there's a search bar and a table displaying network edges. The table has columns for 'from' and 'to'. The data in the table is as follows:

from	to
1	CVP
2	CVP
3	PCWP
4	HIST
5	TPR
6	TPR
7	CO
8	HRBP
9	HRBP
10	PAP

At the bottom of the table, it says 'Showing 1 to 10 of 55 entries'. To the right of the table, there are navigation links for 'Previous' and 'Next'.

Figure S24. tables containing network graph, validation results etc

Publish your dashboard

This section is one of the key highlights of the app. Often user find it difficult effectively communicate their results on bayesian learning. This app enables the user to produce a custom dashboard of their results as an R package.

The user has options to select the name and theme for the dashboard, the app simply builds the dashboard for them which is downloadable as an R package through the app. The custom dashboard is equipped with flagship features of wiseR like the interactive graph exploration and inference learning and visualization.

This feature save author hassle of creating a dashboard for their findings, and helps propagating research output to the community in an efficient manner, which is the main motive behind wiser i.e bridging the gap between the research community and technology.

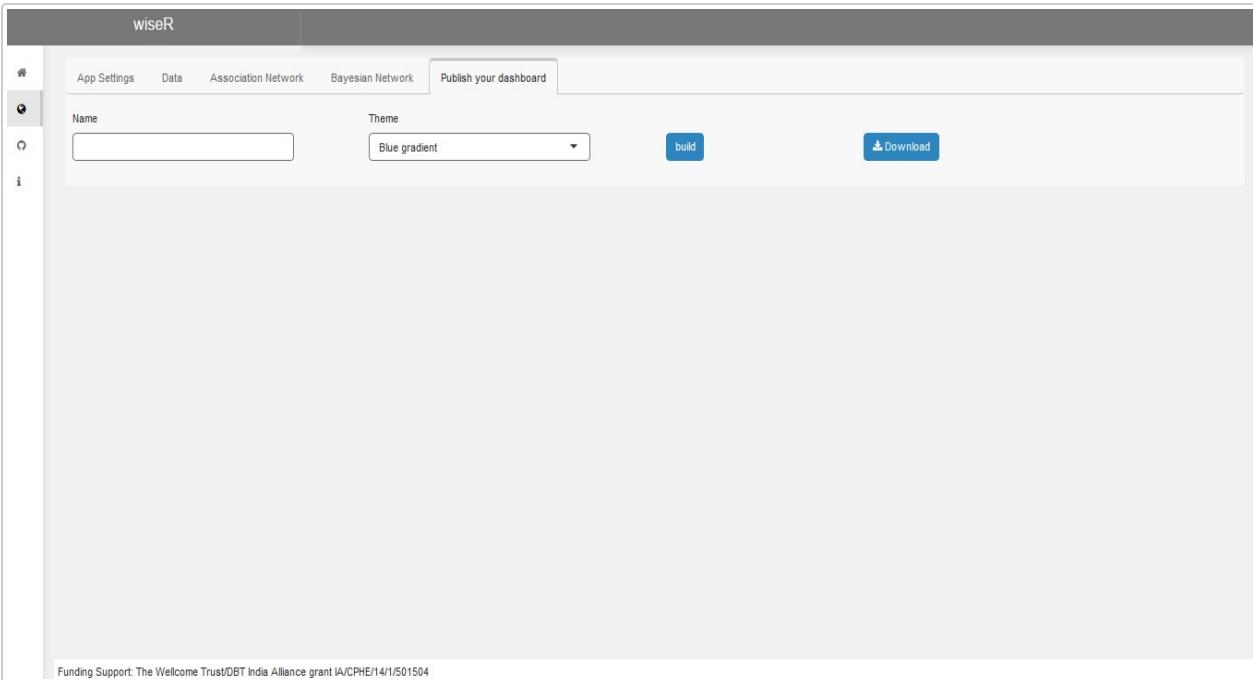


Figure S25. Publish your dashboard

Comparison

We draw a simple comparison of the wiseR app with existing bayesian learning and present it in the table below

Table Key: * Open source (OS): Is the source code available ? If yes what programming language? * Target Audience (TA) :What is the target audience? Based on the source code availability and programming language used, the app can be target to end user, data scientist or both. * Enabled Statistical/ML extensions (MLE) : Does the backend language supports AI/ML libraries for customizations in those directions? * Structure Learning (SL): Is structure learning possible? * Bootstrapped Learning (BL): Is robust bootstrap structure learning possible? * Interventional Data(INT): Can it handle interventional data and incorporate it in structure learning? * Cross Validation(CV): Does the app provides means for cross validation and evaluation of learned models? * Parameter learning(PL): is parameter learning possible using the app? * Informed Layout(IL): is network visualization using a wide variety of efficient and targeted graph layouts for exploration ? * Community Detection (CD) : are subgraphs based on communities/modules detected in the graph using available for visualization and exploration? * Inference with Confidence (IC): Can the app perform inference learning with confidence intervals ? * Chained Inferences(CI): can the app handle multi-evidence inference learning? * Exact Inference(EI): can the app perform exact inference learning? * Approximate Inference with error bars(AIE): can the app perform much faster approximate inferences, verified over multiple iteration and produce final results with error bars(Much faster and equally accurate than exact inference on large datasets)? * Parallel processing(PP) : Does the app enable the user to run the process in parallel for faster runtime? * Free: Is the app free for public use?

A comparison of wiseR and other bayesian learning apps

Name	OS	TA	MLE	SL	BL	INT	CV	PL	IL	CD	IC	CI	EI	AIE	PP	Free
ShinyBN	Yes (R)	Data Scientists,End users	Yes													
Bayesian Networks	Yes (R)	Data Scientists, End users	Yes	Yes	No	No	No	Yes	No	Yes						
BayesiaLab	No	End Users	No	Yes	No	No	No	Yes	No	No	No	Yes	Yes	No	No	No

Name	OS	TA	MLE	SL	BL	INT	CV	PL	IL	CD	IC	CI	EI	AIE	PP	Free
Bayes Server	No	End Users	No	Yes	No	No	No	Yes	No	No	No	Yes	Yes	No	No	No
BNJ	Yes (Java)	End Users	No	No	No	No	No	Yes	No	No	No	No	Yes	No	No	Yes
Clspace	Yes (Java)	End Users	No	No	No	No	No	No	No	No	No	Yes	No	No	Yes	
OpenMarkov	Yes (Java)	End Users	No	Yes	No	No	No	Yes	No	No	No	Yes	Yes	No	No	Yes
Sam Iam	No	End Users	No	Yes	No	No	No	No	No	No	No	Yes	No	No	Yes	
UnBBayes	Yes (Java)	End Users	No	Yes	No	No	No	Yes	No	No	No	Yes	Yes	No	No	Yes

Example

We explain the usefulness of bayesian networks by replicating the results presented in Sachs et al. (2005), which utilizes bayesian learning on complex interventional data.

We upload the Sachs interventional data which is in a space separated text file into the app. Variables are read as factors as it is a numerically encoded discrete data.

The screenshot shows the wiseR web application interface. The top navigation bar includes tabs for 'App Settings', 'Data' (which is selected), 'Association Network', 'Bayesian Network', and 'Publish your dashboard'. Below the navigation is a toolbar with 'Dataset' and 'Explore' buttons, and buttons for 'upload', 'Pre-Process', and 'Download'. A search bar labeled 'Search:' is also present. The main content area displays a table with 10 rows of data and 15 columns, labeled 'Raf', 'Mek', 'Pigc', 'PIP2', 'PIP3', 'Erk', 'Akt', 'PKA', 'PKC', 'P38', 'Jnk', and 'INT'. The table has a light gray background with alternating row colors. At the bottom of the table, it says 'Showing 1 to 10 of 5,400 entries' and includes a page navigation bar with buttons for 'Previous', '1', '2', '3', '4', '5', '...', '540', and 'Next'. A small note at the bottom left states 'Funding Support: The Wellcome Trust/DBT India Alliance grant IA/CPHE/14/1/501504'.

Figure S26. Data uploaded

The variable INT holds interventional information, adjustment is made for the same in the preprocess menu. This will now be used as a part of bayesian structure learning.

The screenshot shows the wiseR interface with several data manipulation tools:

- Convert Variables to Factor:** A dropdown menu set to "Raf" with a "Convert" button.
- Impute Missing Data:** A "Impute" button.
- Discretize Data:** A dropdown menu set to "hybrid discretization(Recommended)" with a "Discretize" button.
- Hartemink Discretization Parameters:** Input fields for "breaks" (5) and "ibreaks" (5).
- Transpose data frame:** A "Transpose" button.

On the right, there is a large table with columns: Akt, PKA, PKC, P38, Jnk, INT. The data is as follows:

	Akt	PKA	PKC	P38	Jnk	INT
1	1	3	1	2	1	8
2	2	3	1	2	1	8
3	1	3	2	1	1	8
4	1	3	1	3	1	8
5	1	3	1	1	1	8
6	1	3	1	2	1	8
7	1	3	1	3	1	8
8	1	3	1	3	1	8
9	1	3	1	1	1	8
10	2	3	1	1	1	8

Navigation buttons at the bottom: Previous, 1, 2, 3, 4, 5, ..., 540, Next.

Figure S27. Handling interventional information

We now learn a simple bayesian network on the data using Hill climbing algorithm and mbde network score. This graph will now be used to initialize structure learning using tabu algorithm. This mechanism of graph initialization in structure learning is especially useful in score-based learning like Tabu, which prevents it from getting stuck in local maxima.

The screenshot shows the wiseR interface with a Bayesian Network tab selected. The network structure is as follows:

```

graph TD
    Event((Event)) --> Raf((Raf))
    Raf --> Erk((Erk))
    Raf --> Akt((Akt))
    Erk --> Akt
    Akt --> Mek((Mek))
    Mek --> PKA((PKA))
    Mek --> PKC((PKC))
    PKA --> Jnk((Jnk))
    PKC --> Jnk
    Jnk --> Plcg((Plcg))
    Plcg --> PIP3((PIP3))
    PIP3 --> PIP2((PIP2))
    PIP2 --> Raf
    PIP2 --> Erk
    PIP2 --> Akt
    PIP2 --> Mek
    PIP2 --> PKA
    PIP2 --> PKC
  
```

Control buttons include: Structure Learning, Inference Learning, Bayesian Network, Publish your dashboard, Nth Neighbors(of selection), Modules: graph, Detect Modules, Visual Settings, Refresh, and Save network.

Funding Support: The Wellcome Trust/DBT India Alliance grant IA/CPhE/14/I/501504

Figure S28. Learn structure using hill climbing

The screenshot shows the wiseR web application interface. The top navigation bar includes tabs for App Settings, Data, Association Network, Bayesian Network (selected), and Publish your dashboard. Below the tabs are buttons for Structure Learning (selected) and Inference Learning, along with links for Bayesian Network, Fitted Local Distributions, Infer Decisions, and Export Tables. A dropdown menu for 'Bayesian Graph' is open, and a 'Download' button is visible. A search bar and a 'Show 10 entries' dropdown are also present. The main content area displays a table of 10 edges from a Bayesian graph:

	from	to
1	Raf	Mek
2	Raf	Erk
3	Raf	Akt
4	Raf	PKC
5	Mek	Plcg
6	Mek	Akt
7	Mek	PKA
8	Mek	PKC
9	Mek	P38
10	Mek	Jnk

Below the table, it says 'Showing 1 to 10 of 27 entries' and has a page navigation section with buttons for Previous, 1, 2, 3, and Next. At the bottom left, there is funding information: 'Funding Support: The Wellcome Trust/DBT India Alliance grant IA/CPHE/14/1/S01504'.

Figure S29. Download netowrk graph as csv

We now upload the graph as initialization for structure learning.

The screenshot shows the wiseR interface with the 'Structure Learning' tab selected. The top navigation bar and tabs are identical to Figure S28. The main area features a 'Structure Learning' panel with buttons for Initialize Structure (optional), Learn Structure, Upload Pre-learnt Structure, Edit Structure (optional), Validate Structure, Select Modules, Visual Settings, and Refresh. Below this is a 'Upload list of prior known edges (as CSV)' section with a 'Browse...' button, a highlighted 'Bayesian Graph.csv' file, and an 'Upload complete' message. To the right is a network graph visualization with nodes: Akt, Erk, Raf, Mek, PKC, Plcg, and PIP2. Edges are shown between Raf and Mek, Raf and Erk, Raf and Akt, Raf and PKC, Mek and Plcg, Mek and Akt, and Mek and PIP2. On the left, there are controls for adding edges ('from' and 'to' dropdowns, 'Add' button, 'Show 10 entries' table), removing/reversing edges, and a search bar. At the bottom right are icons for saving the network and other controls.

Figure S30. Initialize a new structure using the previous graph

We now set the appropriate parameters for structure learning.
 * Algorithm: tabu
 * Network score: modified bayesian dirichlet equivalent
 * ISS(imaginary sample size): 15
 * Parameter fitting algorithm: bayesian parameter estimation

We perform a simple bayesian learning using tabu, to replicate the results. User can select the bootstrap parameters and do a bootstrap learning, to produce more robust structures.

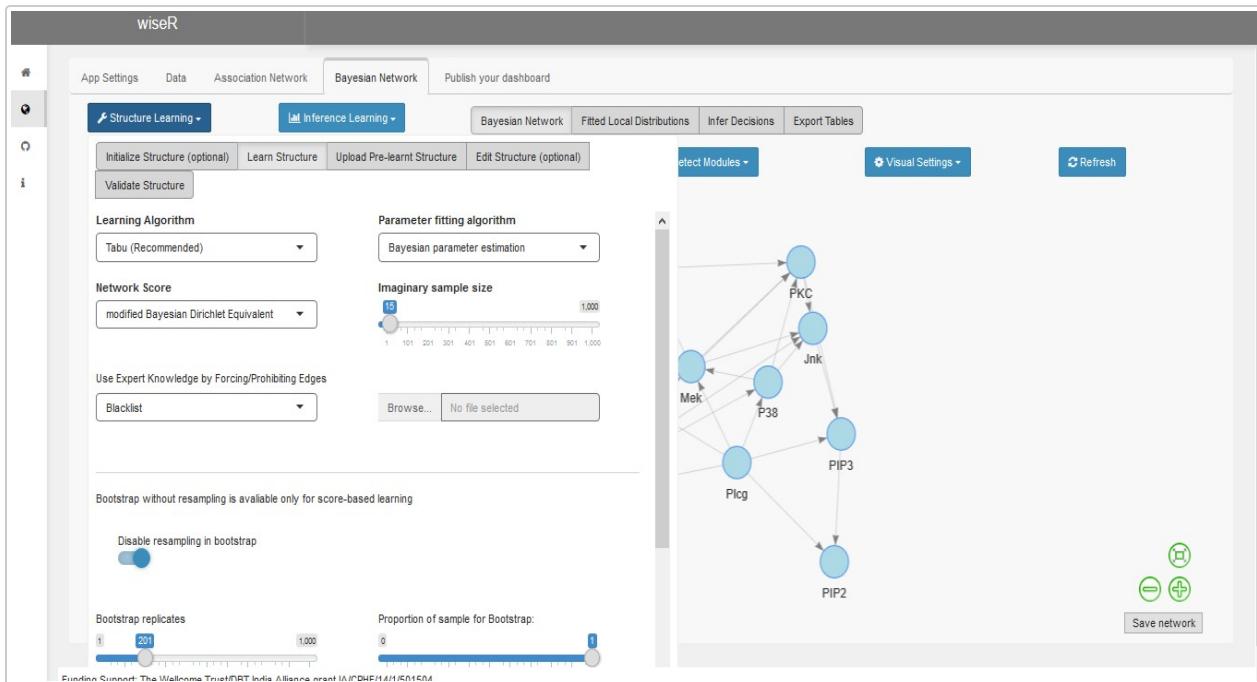


Figure S31. Structure learning using tabu algorithm

As we can see, the final produced structure has all the validated arcs that are present in the original paper even though a few have been reversed. The structure contains some unvalidated arcs as well which were discovered in the original paper but discarded due to low confidence.

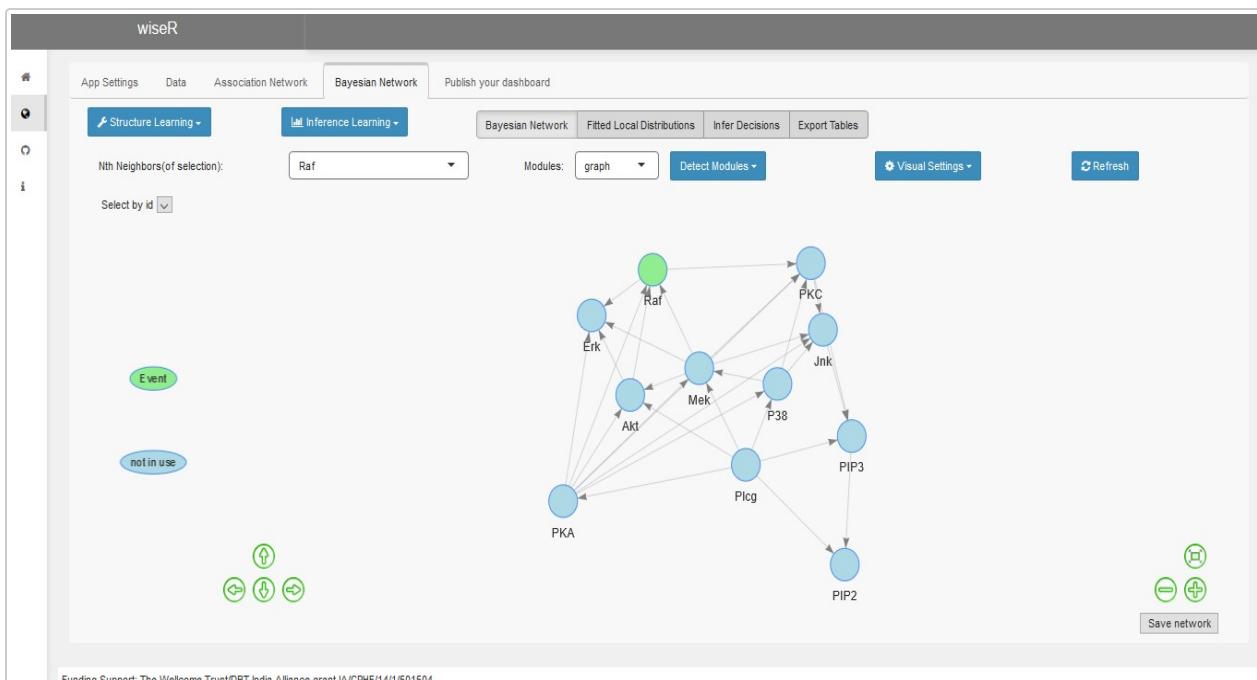


Figure S32. Final learned structure

We now confirm exact inference results with approximate inference with error bar to show that the unique approximate inference mechanism provided in the app produces as accurate results as exact inference without computational constraints in case of large structures. For this purpose we set the node 'Akt' as event conditional on 'Erk = 1'. In the probability plots produced we can clearly see that approximate inference with error bars produces as accurate results as exact inference within 0.05 range of error, which is negligible

Exact Inference

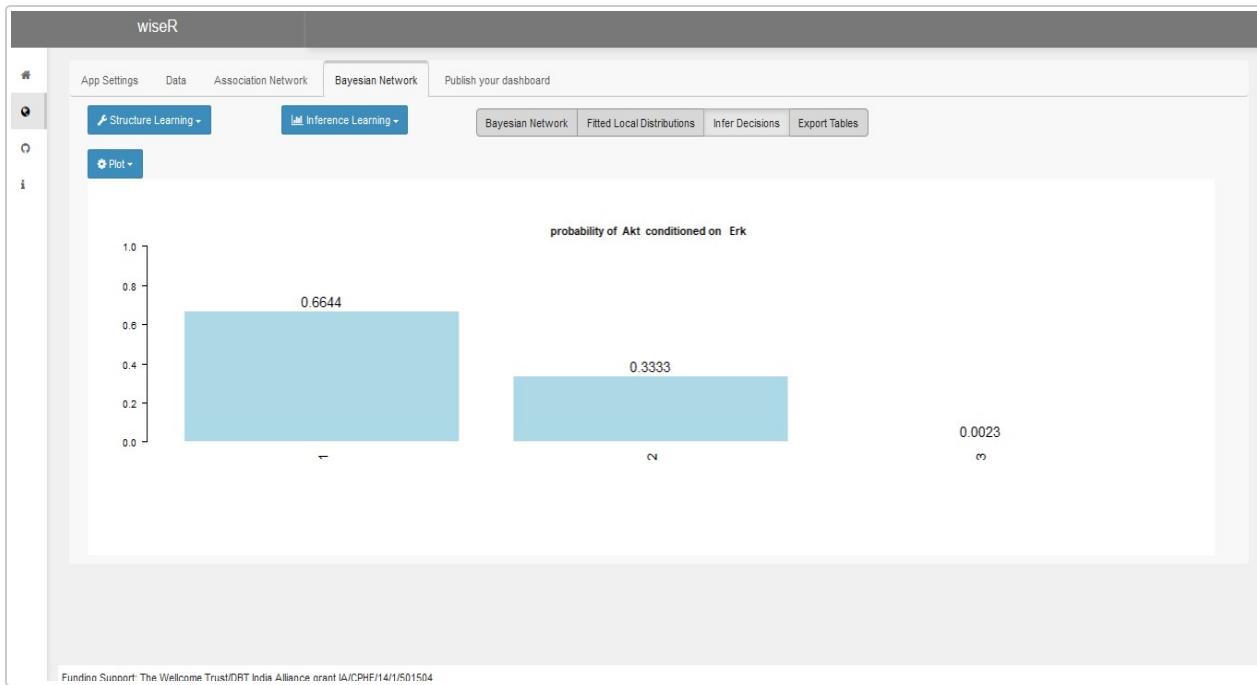


Figure S33. Exact inference plot

Approximate Inference with error bars

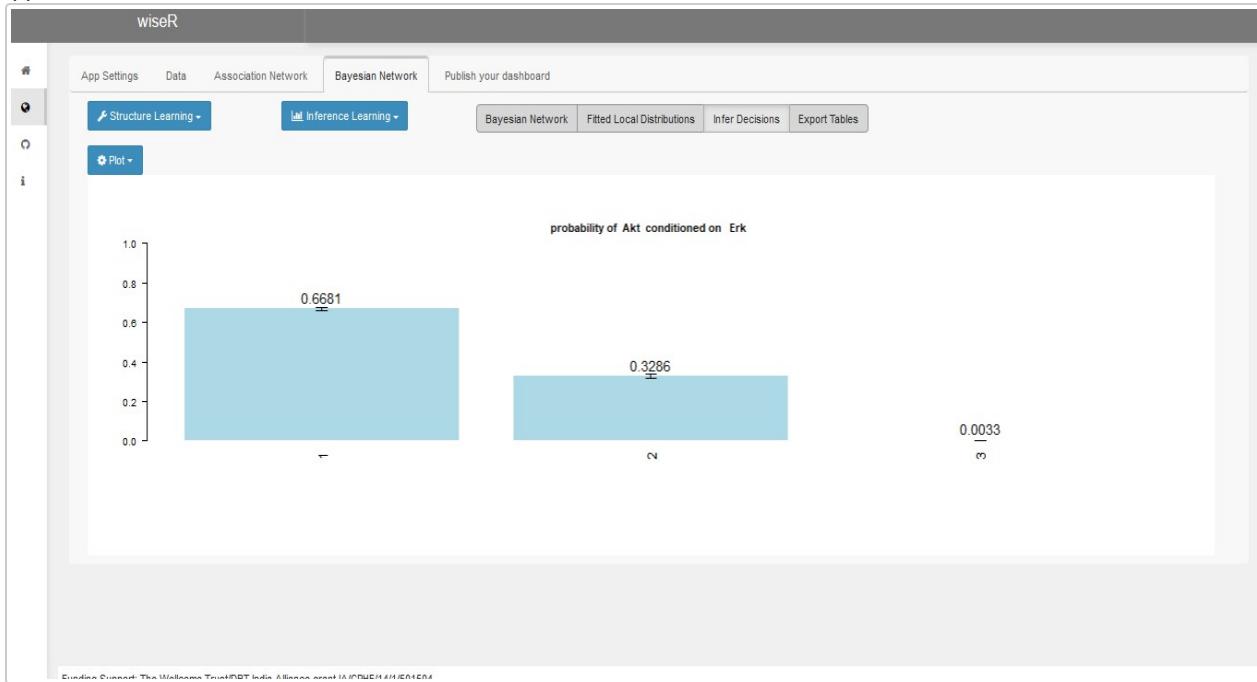


Figure S34. Approximate inference plot

Powered by

The wiseR engine depends upon the following awesome libraries

- *RBGL* (Vince Carey, Li Long and R. Gentleman (2017). RBGL: An interface to the BOOST graph library. R package version 1.52.0. <http://www.bioconductor.org>)
- *graph* (R. Gentleman, Elizabeth Whalen, W. Huber and S. Falcon (2017). graph: graph: A package to handle graph data structures. R package version 1.54.0.)
- *bnlearn* (Marco Scutari (2010). Learning Bayesian Networks with the bnlearn R Package. Journal of Statistical Software, 35(3), 1-22. URL <http://www.jstatsoft.org/v35/i03/>.)
- *rhandsontable* (Jonathan Owen (2018). rhandsontable: Interface to the 'Handsontable.js' Library. R package version 0.3.6. <https://CRAN.R-project.org/package=rhandsontable>)
- *shiny* (Winston Chang, Joe Cheng, JJ Allaire, Yihui Xie and Jonathan McPherson (2017). shiny: Web Application Framework for R. R package version 1.0.5. <https://CRAN.R-project.org/package=shiny>)
- *shinydashboard* (Winston Chang and Barbara Borges Ribeiro (2017). shinydashboard: Create Dashboards with 'Shiny'. R package version 0.6.1. <https://CRAN.R-project.org/package=shinydashboard>)
- *dplyr* (Hadley Wickham, Romain Francois, Lionel Henry and Kirill MÃ¼ller (2017). dplyr: A Grammar of Data Manipulation. R package version 0.7.4. <https://CRAN.R-project.org/package=dplyr>)
- *visNetwork* (Almende B.V., Benoit Thieurmel and Titouan Robert (2018). visNetwork: Network Visualization using 'vis.js' Library. R package version 2.0.3. <https://CRAN.R-project.org/package=visNetwork>)
- *shinyWidgets* (Victor Perrier and Fanny Meyer (2018). shinyWidgets: Custom Inputs Widgets for Shiny. R package version 0.4.1. <https://CRAN.R-project.org/package=shinyWidgets>)
- *missRanger* (Michael Mayer (2018). missRanger: Fast Imputation of Missing Values. R package version 1.0.2. <https://CRAN.R-project.org/package=missRanger>)
- *tools* (R Core Team (2017). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>.)
- *shinyalert* (Dean Attali and Tristan Edwards (2018). shinyalert: Easily Create Pretty Popup Messages (Modals) in 'Shiny'. R package version 1.0. <https://CRAN.R-project.org/package=shinyalert>)
- *shinycssloaders* (Andras Sali (2017). shinycssloaders: Add CSS Loading Animations to 'shiny' Outputs. R package version 0.2.0. <https://CRAN.R-project.org/package=shinycssloaders>)
- *rintrojs* (Carl Ganz (2016). rintrojs: A Wrapper for the Intro.js Library. Journal of Open Source Software, 1 (6), October 2016. URL <http://dx.doi.org/10.21105/joss.00063>)
- *arules* (Michael Hahsler, Christian Buchta, Bettina Gruen and Kurt Hornik (2018). arules: Mining Association Rules and Frequent Itemsets. R package version 1.6-1. <https://CRAN.R-project.org/package=arules>)
- *psych* (Revelle, W. (2018) psych: Procedures for Personality and Psychological Research, Northwestern University, Evanston, Illinois, USA, <https://CRAN.R-project.org/package=psych> Version = 1.8.4.)
- *DescTools* (Andri Signorell et mult. al. (2018). DescTools: Tools for descriptive statistics. R package version 0.99.24.)
- *DT* (Yihui Xie (NA). DT: A Wrapper of the JavaScript Library 'DataTables'. R package version 0.4.11. <https://rstudio.github.io/DT>)
- *linkcomm* (Kalinka, A.T. and Tomancak, P. (2011). linkcomm: an R package for the generation, visualization, and analysis of link communities in networks of arbitrary size and type. Bioinformatics 27 (14), 2011-2012.)
- *igraph* (Csardi G, Nepusz T: The igraph software package for complex network research, InterJournal, Complex Systems 1695. 2006. <http://igraph.org>)
- *parallel* (R Core Team (2017). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <https://www.R-project.org/>.)
- *snow* (Luke Tierney, A. J. Rossini, Na Li and H. Sevcikova (2016). snow: Simple Network of Workstations. R package version 0.4-2. <https://CRAN.R-project.org/package=snow>)
- *shinyBS* (Eric Bailey (2015). shinyBS: Twitter Bootstrap Components for Shiny. R package version 0.61. <https://CRAN.R-project.org/package=shinyBS>)

- *gRbase* (Claus Dethlefsen, Søren Højsgaard (2005). A Common Platform for Graphical Models in R: The gRbase Package. *Journal of Statistical Software*, 14(17), 1-12. URL <http://www.jstatsoft.org/v14/i17/>.)
- *gRain* (Søren Højsgaard (2012). Graphical Independence Networks with the gRain Package for R. *Journal of Statistical Software*, 46(10), 1-26. URL <http://www.jstatsoft.org/v46/i10/>.)