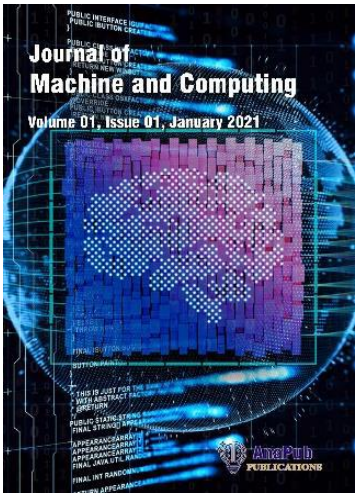
Journal Pre-proof

Bayesian Network Meta-Analysis of Survival Data using a Near-Ignorance Dirichlet Process with Pseudo-IPD



Amritendu Bhattacharya, Ravilisetty Revathi and Boya Venkatesu

DOI: 10.53759/7669/jmc202505088
Reference: JMC202505088
Journal: Journal of Machine and Computing.

Received 23 May 2024
Revised form 26 October 2024
Accepted 10 March 2025

Please cite this article as: Amritendu Bhattacharya, Ravilisetty Revathi and Boya Venkatesu, “Bayesian Network Meta-Analysis of Survival Data using a Near-Ignorance Dirichlet Process with Pseudo-IPD”, Journal of Machine and Computing. (2025). Doi: https:// doi.org/10.53759/7669/jmc202505088

AnaPub
PUBLICATIONS

Bayesian Network Meta-Analysis of Survival Data Using a Near-Ignorance Dirichlet Process with Pseudo-IPD

[1]Amritendu Bhattacharya, [2]Ravilisetty Revathi, [3]Boya Venkatesu
[1] School of Technology, Woxsen University, Telangana, India-502345
[2] School of Sciences, Woxsen University, Telangana, India-502345
[3] School of Business, Woxsen University, Telangana, India-502345

[1]amri10du@gmail.com , [2]revathiravilisetty@gmail.com , [3]venkateshboya50@gmail.com

Correspondence should be addressed to Ravilisetty Revathi : revathiravilisetty@gmail.com

Abstract - Among the few approved therapies for advanced renal cell cancer, Sunitinib is a commonly active comparator in most trials. The pembrolizumab-plus-axitinib and nivolumab-plus-cabozantinib combination therapies have shown better efficacy compared to Sunitinib in different studies but there is no direct head-to-head study between the two combination therapies. Network Meta Analysis is employed to compare the treatments indirectly. Usually, the aggregate Hazard ratio-based approach and endpoints are used in Network Meta Analysis. Matching Adjusted Indirect Comparison has been reported for checking these two sets of combination therapies. Proportionality assumption violation is an issue with using Cox proportional hazard ratio while Matching Adjusted Indirect Comparison is not free of bias. We therefore employ pseudo-Individual patient level data generated from digitized survival curves and apply a new prior near-ignorance Dirichlet Process. We then compare the results of cox-regression based method and a Bayesian approach based on near ignorance imprecise prior Dirichlet Process with Pseudo-IPD based Network Meta Analysis. Based on both the Cox-regression and pseudo-IPD based-approaches, there is no statistically significant difference between the two groups based on efficacy. Both the combination therapies perform significantly better than Sunitinib arm in term of efficacy when using the Overall Survival and Progression free Survival endpoints. Since the Bayesian prior near-ignorance Dirichlet Process based method does not assume proportionality, it is a better choice. In the current work, a R software-based analysis is done with an example dataset to compare and present the results from the two methods.

Keywords - Dirichlet process, Network meta analysis, Restricted mean survival time, Progression free survival, Matching adjusted indirect comparison, pseudo-Individual Patient Data

I. INTRODUCTION

Renal cell cancer (RCC) contributes close to 2 percent of all diagnosed cancer cases and the rate is increasing year on year [1]. Clinicians classify RCC into different stages and the Stage 4 where the cancer spreads to distant organs are referred to as advanced renal cell cancer (ARCC). ARCC has less than 10 percent average 5-year survival rate in contrast with over 70 percent average 5-year survival rate in all RCCs [2].

Apart from nephrectomy surgery and radiotherapy, immunotherapy has been approved in the last decade. Sunitinib, a vascular endothelial growth factor receptor inhibitor was approved in 2017 followed by several others. Even though Sunitinib is considered the standard first line immunotherapy, few combination therapies such as pembrolizumab-plus-axitinib and nivolumab-plus-cabozantinib have shown better efficacy in head-to-head trials with Sunitinib arm in the Keynote-426 and Checkmate trials respectively.

There are no head-to-head clinical trial between the pembrolizumab-plus-axitinib and nivolumab-plus-cabozantinib combination therapies for ARCC. The ICER/QALY based on incremental cost-effectiveness ratios (ICERs) and quality-adjusted life-years (QALYs) is very different for the two studies. At ICER of 508,987/QALY as reported by Sin Li et al [3], the nivolumab-plus-cabozantinib combination seems more costly than the pembrolizumab-plus-axitinib combination as it has a lower ICER of USD 148,676/QALY as reported by Ding et al [4]. A Matching Adjusted Indirect Comparison (MAIC) study showed the nivolumab-plus-cabozantinib to be statistically significant in terms of Overall survival and Progression free survival over pembrolizumab-plus-axitinib [5]. In MAIC however, full patient level data was taken from CheckMate-426 trial and reweighted before comparing with the aggregate level data of Keynote study. It could be susceptible to bias as data from one study are purely excluded on the basis of few demographic or study level characteristics. Therefore, it is important to know the comparative efficacy benefits of each of the two combination therapies. Until a head-to-head trial result are out, an indirect comparison of the data via a common reference arm could

provide a good insight into the efficacy aspects. In this study we have generated pseudo-individual patient data from the Kaplan-Meier plots of overall survival (OS) and progression free survival (PFS) and using the common Sunitinib as active reference arm, computed an indirect treatment difference estimate using the imprecise Dirichlet Process based survival analysis. There are other potential combination therapies such as pembrolizumab-plus-lenvatinib but for the sake of demonstration, we have restricted the analysis to the two trials data.

II. LITERATURE REVIEW

Data analysis based on duration of time to a defined event of interest falls under the broad category of lifetime data analysis or survival analysis. Survival analysis, is widely employed in lifetime outcomes evaluation in clinical trials. They have been applied in several other domains such as financial risk assessment as well as churn data in marketing. In survival analysis, Hazard Ratio (HR) is a widely used estimate as input for Meta-Analysis and Network Meta-Analysis (NMA). While MA combining trials that contrast same set of two treatment arms, there are many important treatment differences that are of interest but unavailable due to lack of head-to-head clinical trial. NMA are employed in such scenarios to combine trials data as long as there is a common connecting treatment node across trials. In the field of evidence synthesis, results from several different experiments or clinical trials of similar designs are often clubbed together based on a fixed set of inclusion and exclusion criteria to refine and obtain overall estimates.

Though most trials do not provide access to the survival dataset, results usually include the Kaplan Meier survival plot. Digitization software such as 'IPDfromKM' and 'DigitizeIt' allow us to approximately obtain the de-identified Individual patient data adjusted for right-censored events.

In specific oncological therapeutic areas such as Renal cancer, many alternative drugs are approved or in advanced phase of clinical trials but lack of direct head-to-head studies between important competitors is a hindrance in estimating their relative treatment effects.

In Frequentist framework the survival models are grouped as non-parametric, semi-parametric and parametric models [6]. Kaplan–Meier estimator [7] is an example of a non-parametric method. The cox-proportional model is a semi-parametric model in which one or more co-variates predict the hazard function and event rate. Cox-regression models have been the mainstay of survival analysis over the last few decades. However non-proportionality of hazard between the 2 treatment arms is a drawback and challenge in clinical data. Also, interaction effects among co-variates adversely impact the assumption of linear relation between co-variates and the log of the relative hazard and make the proportional hazard assumption very subjective [8]. The parametric models such as those based on Gompertz, Weibull and exponential are a better option if the distribution is followed but any deviation from the assumed distribution hampers their adaptability to diverse datasets [9].

The Bayesian framework have been applied to model survival data. Both the parametric Bayesian approaches and Non-parametric Bayesian approaches have been in practice. The Bayesian framework have benefits such as its flexibility to incorporate external data and continual monitoring and updating of data. Bayesian estimation can potentially assimilate external or historic data in the form of prior distributions. Integrating relevant historic data leads to improvement in estimate precision and overcoming small sample size issues and have been recommended.

Bayesian parametric survival models were shown to be equivalent to conventional survival models with minimal hyperparameter tuning, overcoming the problem of model overfitting and quantifying the level of uncertainty on the inference.

There are many recent advances in survival analysis. Federated survival analysis based on Dirichlet distribution have been applied on distributed data while retaining user privacy. A variational Bayes autoencoder for survival analysis has been implemented by Apellániz et al. [10]. Threshold regression, and its modified versions have been around since more than a decade.

In terms of estimate endpoints, Restricted Mean Survival Time (RMST) that have emerged as an alternative to Cox Proportional Hazard Ratios and Parametric Hazard Ratios.

Most clinical trial results provide the survival plots which contain the Kaplan Meier survival curves along with number os subjects at risk and events at specific intervals along the trial duration. The Guyot al algorithm, and its modified versions can approximately reproduce the de-identified individual patient data (IPD) [11]. The data generated has the event and censoring information for all subjects in the original trial data without linking the event to actual subject on the lines of exchangeability.

In the current work we combine data from 2 different clinical trial on ARCC, each of which have the approved Sunitinib treatment arm. 2 different drug combinations, namely, Pembrolizumab plus Axitinib and Nivolumab plus Cabozantinib are approved for the ARCC as well but do not have many head-head trial. However, we have here the two trial results where each of these combinations have been tested against the Sunitinib.

If we combine the data of the 2 trials, then the 2 combination therapies can be compared indirectly via the Sunitinib reference arm. However, in case of heterogeneity in the Sunitinib arm across the 2 studies can impact the interpretation.

We suggest 2 approaches. In case there is no statistical difference across the 2 studies in Sunitinib Survival rate based on the log-rank test, we can perform a Frequentist NMA. However, in scenarios where there is heterogeneity, the use of Dirichlet Process based analysis is a potential solution. The imprecise Dirichlet Process prior based approach of Mangili et al is used to obtain a posterior distribution of the survival curve. The application of imprecise Dirichlet model estimating lifetimes in presence of right-censored data is well established. The basis of imprecise Dirichlet model in cases with incomplete observation in failure data have also evolved over time.

If, in two similar trials data, there is one common treatment arm in both studies with statistically similar survival trends, we can assume robust treatment contrast between the two non-common treatment arms via indirect network.

The inclusion criteria should be based on disease stage, endpoint, trial phase, demographic variables such as age-range and gender ratio of included participants in the trial among others. The exclusion could be based on features such as bio-naive versus bio-experienced population features in the different studies that could potentially be added for NMA or in building the reference arm. Such criteria need to defined prior to start of the NMA.

Susarla et al developed a non-parametric Bayesian estimator of the survival curve using a squared-error loss function using DP prior which was a Bayesian equivalent of the Kaplan-Meier estimator [12]. Bayesian estimates perform well with heterogeneous and hierarchical data. An issue that has persisted in this is the choice of infinite-dimensional parameter (base measure) when prior information is limited. In this work we utilize the Imprecise DP (IDP)—a prior near-ignorance DP-based model developed by Mangili et al as it does not require this probability measure [13]. It essentially utilizes a multinomial distribution with Dirichlet priors, thereby introducing nonparametric bayesian approach.

III. METHODOLOGY

Dirichlet distribution finds application in several areas including clustering, meta-analysis, and time-to- event survival analysis. It is finding increasing utilized in Bayesian and non-parametric inference. The Dirichlet distribution Dir() is a family of continuous multivariate probability distributions parameterized by a vector of positive reals. It is a multivariate generalization of the Beta distribution. The Dirichlet process is the infinite-dimensional generalization of the Dirichlet distribution. While Dirichlet distribution are applied as conjugate prior for the categorical distribution, the Dirichlet process are utilized as conjugate prior for infinite, nonparametric discrete distributions.

Dirichlet distribution, named after Johann Gustav Dirichlet, a Mathematician, is also known as Multivariate Beta distribution (MBD) [14] of which beta distribution is a special case [15] when there are two possible, mutually exclusive outcome events that add up to one. A Dirichlet distribution can be used to model random probability mass functions (pmfs) for finite set of outcomes. Let us assume there is a set of vectors of outcomes X_1, X_2, ..., X_n which are positive numbers that together add up to one. This vector set follows a Dirichlet distribution. The beta distribution is simply a special case when n=2.

The parameters $\alpha_1, \alpha_2, \ldots, \alpha_k$ are positive and equivalent to α and β components of a beta distribution.

Dirichlet distribution is a natural fit to model compositional data and in Bayesian analysis [16]. Several studies observe that the Dirichlet distribution provides a convenient prior for Bayesian analyses involving multinomial proportions [17]. In addition, Dirichlet distribution has wide range of applications in diverse fields such as forensic sciences, statistical genetics, health economic modeling as well as in consumer behavior pattern analysis. Dirichlet distributions have also been to accurately model proteins utilizing the data of component molecules of the protein over different organelle. In other words, Dirichlet distributions are a category of probability distributions that are defined on a simplex. A probability mass function with n components lie on a (n-1) dimensional probability simplex denoted by Δn whose positive only n-component sum up to one. While the components Δn lies in a n-dimensional space, the Δn is itself a $\Delta(n-1)$ dimensional object.

When n =2, the probability lies on a one-dimensional straight line with 2 possible outcome events at the extreme ends of the line. When n=3, the probability simplex is a triangle and when n=4, the probability simplex is a tetrahedron.

The alpha is the concentration or shape parameter of the Dirichlet distribution. The figure from left to right attempt to provide a general idea of the display the probability of outcome for a n=3 component Dirichlet distribution where α_1, α_2 , α_3 are (1,1,1), (9,9,9) and (0.1,0.1,0.1) using an illustrative sketch (from left to right in Figure 1).

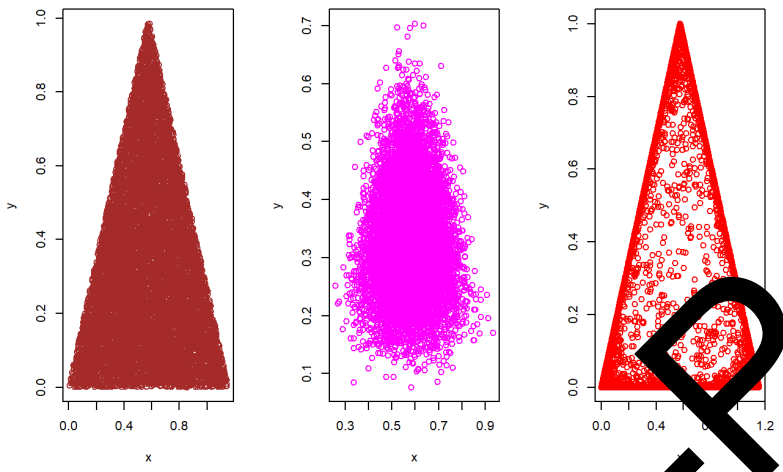


Figure 1: Ternary Dirichlet plot with n=

As the α increases, the values tend to converge towards the centre while they tend to lie of the boundary edges as the α decreases. Different combinations create the various possible distribution patterns.

It is hard to display the equivalent distribution in a tetrahedron but the basis is similar. A (0.1, 0.1, 0.1, 0.1) would have the events space closer to the edges. All vertices are equidistant from one another and hence it is of a tetrahedron shape and not a square. The Figure 2 below shows the plot of the tetrahedron.

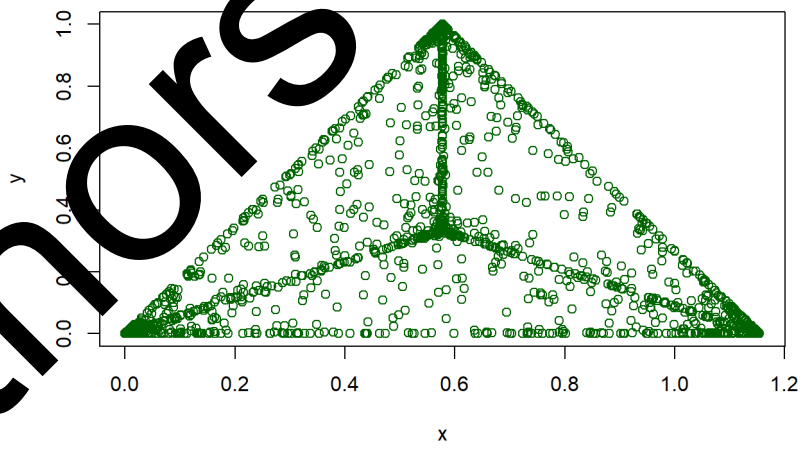


Figure 2: Quaternary Dirichlet Plot with n=4

Dirichlet distribution is strong and does suffer from the limitations bounded by the assumption of finite set of events [18]. Let us say we ask people to state their favorite breakfast item and give them a fixed set of choices: Sandwich, Oats, Idli, Poha, Dosa, Poori and Utthapam. The answers might differ as per mental state and timing of day or week of questioning. This would generate the pmfs to model the probability of choices of individuals. However, this set of choices is restrictive as there are plenty more food options that could be options if there was no restriction. In order to model pmfs over potentially infinite options, we need a distribution over distributions which we know as Dirichlet Process, over an infinite sample space [18]. If we aggregate components of Dirichlet distribution is end up with a new Dirichlet distribution. This

aggregating quality is also true for Dirichlet Process and hence by clubbing outcome categories we can end with having manageable numbers of infinite options.

Thomas S. Ferguson, who introduced the concept of Dirichlet Process, observed that a Dirichlet process is one, where the marginal with respect to any finite partition is a Dirichlet Distribution [19]. It is a random discrete distribution which is nothing short of a revolution in nonparametric Bayesian statistics. The Dirichlet process has a powerful role as a prior in Bayesian analysis [20].

Ferguson showed Dirichlet Process as a prior on probability measures space on a any measurable space (Θ , $B(\Theta)$, where Θ is a complete and separable space and $B(\Theta)$ is a σ-field on X [21]. Dirichlet distribution on the simplex is the natural conjugate prior.

Dirichlet distribution on the simplex is the natural conjugate prior. As per Ferguson, it is a random measure P on measurable space $(\Theta, B(\Theta))$ that has a Dirichlet process prior $D\alpha$ with base measure α if for every finite measurable partition $A_1,..., A_k$ of X, $(P(A_1),...,P(A_k)) \sim Dir(k; \alpha(A_1), ..., \alpha(A_k))$, where $\alpha(.)$ represents a finite positive Borel measure on X.

A Dirichlet Process is a distribution over probability measures such as densities, distributions and masses.

In simple terms, Dirichlet Process is a 2 parameters (α, B_0), with α is the concentration or inverse variance parameter and B_0 is the base distribution.

Its application in text mining and bioinformatics has led to several breakthroughs. Traditional parametric Machine learning models suffer from either overfitting or underfitting. While the Bayesian non-parametric gets over the problem of underfitting using unbound complexity, its ability to approximate the full posterior lessens the chances of overfitting.

The Dirichlet process (DP) is a widely popular BNP model for random probability measures (RPM). The Dirichlet process prior based Bayesian Nonparametric analysis have been in use since 1973 when they were developed by Thomas Ferguson. Bayesian nonparametric stick-breaking aspect of Dirichlet process has been used for building a time-to-event clustering and predictive model that helps identify subpopulation based on risk profiling and individualized time-to-event distributions conditioned on covariates.

Advances using Dirichlet process such as Dirichlet Process Mixture models, the Hierarchical Dirichlet and Latent Dirichlet Allocation have added value in recurrent event modeling, unsupervised clustering/data partitioning and natural language processing respectively. Utilizing Dirichlet process mixture prior relaxes the parametric assumptions, allowing the model to adapt and decipher the relationship between the historic and current control data as well as accounting for the heterogeneity among historic data. Dirichlet regression techniques have found application in compositional data analysis in the presence of an observed covariate [22].

Mangili et al have developed a Dirichlet process with near-ignorance prior approach for deriving survival functions from data that had right censoring that had the advantages of Bayesian inference without the requirement of infinite-dimensional parameters associated with Dirichlet Process [13]. We use their approach to conduct a NMA to retain the benefits of robustness based on prior dependent decisions using the IDP Survival package in R developed by Mangili et al [13].

3.1. NMA based on Survival Analysis Data

NMA can synthesize estimates of treatment differences based on both direct and indirect evidence via results of Randomized controlled trials in clinical settings.

The synthesis of survival time based estimates of treatment effects is usually done by comparison of hazard ratios (HR) based on the Cox proportional hazards regression model [8]. Alternate frailty models and accelerated failure time models have also been used.

NMA based on the Cox regression hazard models are relatively common. NMA have also been performed using fractional polynomials, parametric hazard models and RMST based estimates.

3.2. Real Time dataset for the NMA

As a case study, Kaplan Meier plot results from 2 different phase III clinical trials of ARCC, are used for analysis. Both trials used have a common Sunitinib treatment arm. Subject and study level heterogeneity is expected and NMA models take them into account by using random effects models. We restricted the example dataset to 2 trials and checked for statistically significant difference in the Sunitinib arm across both studies, for easier comprehension and comparison of the other treatment arms. The network is similar to a network proposed by Bucher et al [23]. The reconstructed survival data of individual patient data have been used from published plots of overall survival and progression free survival endpoints of the clinical trials CheckMate and Keynote-426.

The Chekmate clinical trial is a Phase III trial "Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma".

The Keynote-426 clinical trial is a Phase III trial "Nivolumab plus Cabozantinib versus Sunitinib for Advanced Renal-Cell Carcinoma".

The demographics of age and gender were similar in the two studies.

Table 1: Clinical Trials Demographics

Trial	Treatment	Age	Gender
Keynote-426	Pembrolizumab + Axitinib	62 (30–90)	Male 71.3 Female 28.7
	Sunitinib	61 (23–90)	Male 74.6 Female 25.4
CheckMate	Nivolumab + Cabozantinib	62 (23–88)	Male 77.1 Female 22.9
	Sunitinib	61 (28–86)	Male 70.7 Female 29.3

IV. NETWORK META ANALYSIS

The Overall Survival and Progression Free Survival (PFS) endpoint-based survival plots by treatment arm are input in DigitizeIt software to obtain the data points in XY-axis. The data along with the available intervals level information on events is fed into IPDfromKM.

The KM plot of the Keynote-426 is provided below in Figure 3 for the PFS endpoint. A significant difference between the 2 treatment arms and the HR is very close to the original HR reported by the trial.
The reference arm Sunitinib is represented by stata=0. The other active comparator groups in head-to-head trial with Sunitinib have been represented by strata=1.

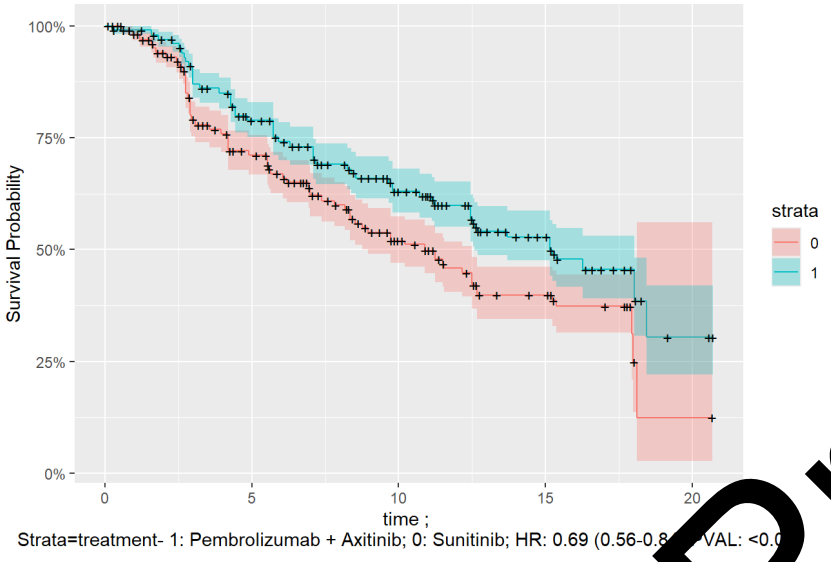


Figure 3: KM Plot: From Keynote-426 reconstructed data on PFS endpoint

The KM plot of the Keynote-426 is provided below in Figure 4 for the OS endpoint. The HR were closely matching the original results of the trial data.

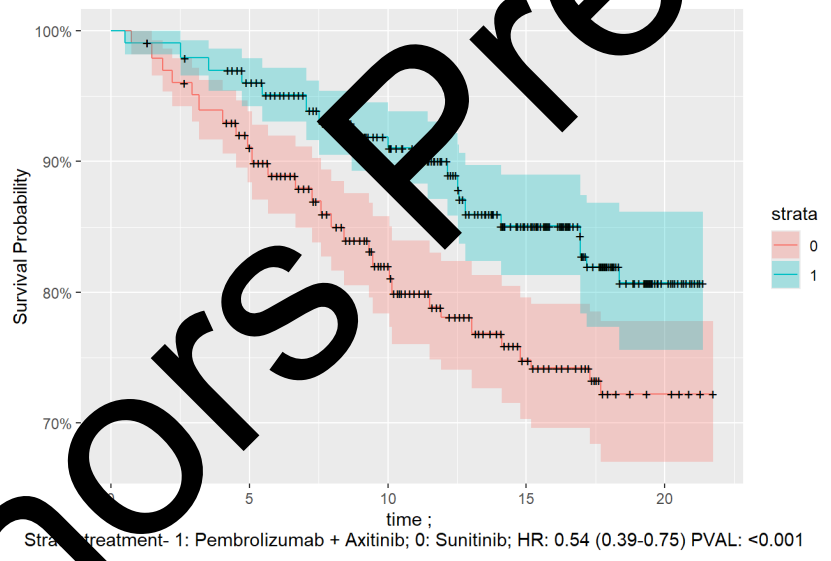


Figure 4: KM Plot: From Keynote-426 reconstructed data on OS endpoint

The KM plot of the CheckMate in Figure 5 shows significant difference between the 2 treatment arms and the HR is very close to the original HR reported by the trial for the PFS endpoint.

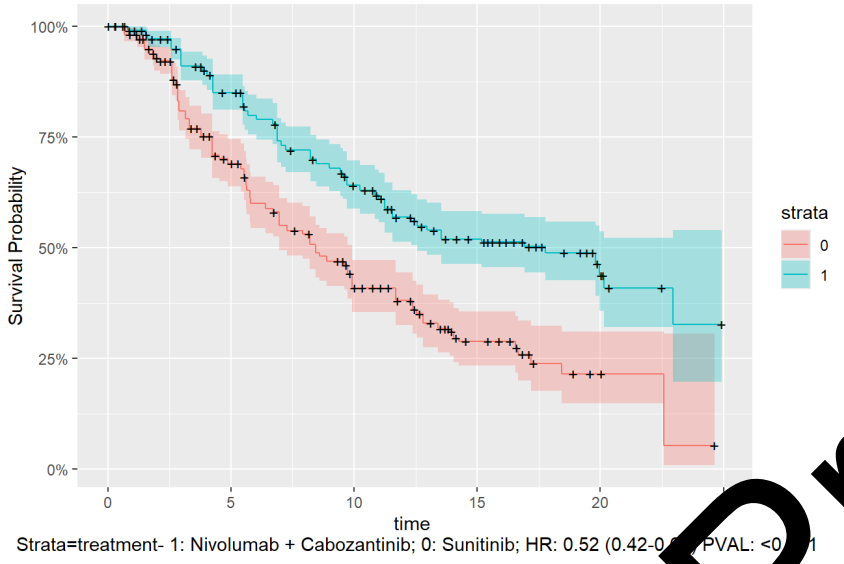


Figure 5: KM Plot: From CheckMate reconstructed data on PFS endpoint

The KM plot of the CheckMate in Figure 6 is provided below for the OS endpoint. The HR were closely matching the original results of the trial data

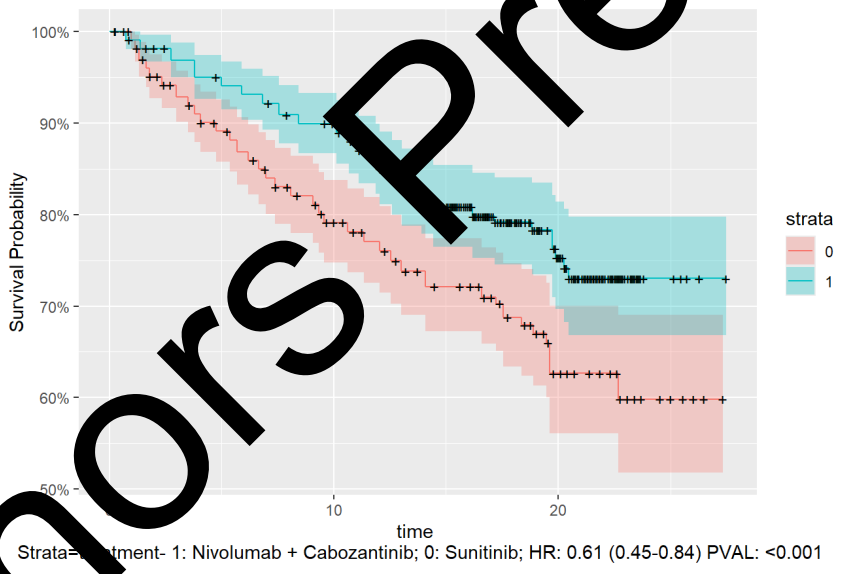


Figure 6: KM Plot: From CheckMate reconstructed data on OS endpoint

To check the heterogeneity in survival across the Sunitinib arm of 2 trials, we generated and checked for any difference via log-rank test on both the endpoints of OS and PFS in Figure 7 and 8 respectively.

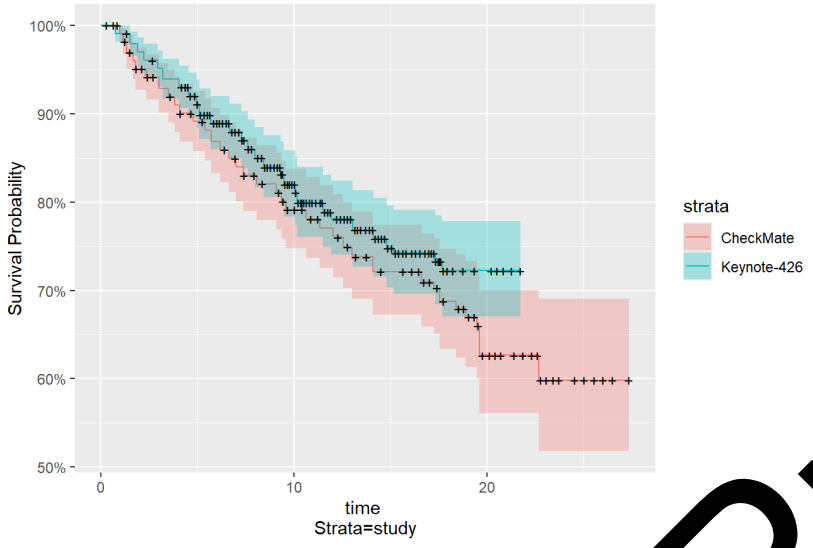
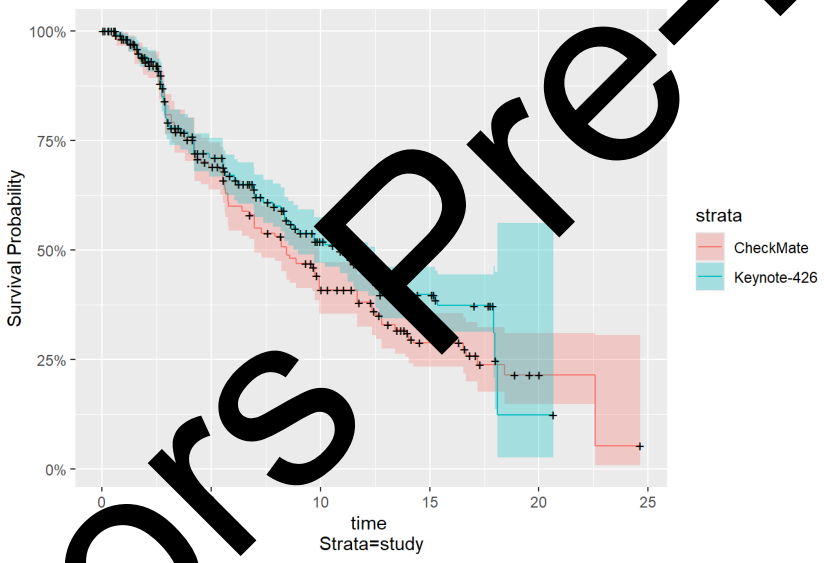


Figure 7: Survival Plot by Sunitinib arm for the 2 studies for O[illegible]point



[illegible]ure [illegible] Sur[illegible]val Plot by Sunitinib arm for the 2 studies for PFS endpoint

The data of the 2 s[illegible]dies were [illegible]mbined and the Sunitinib arm data was considered as one overall group.

The Kaplan M[illegible]r plot a[illegible]d Hazard Ratio of Pembrolizumab plus Axitinib with respect to Nivolumab plus Cabozantinib is presented [illegible]r Overa[illegible]l Survival in Figure 9.

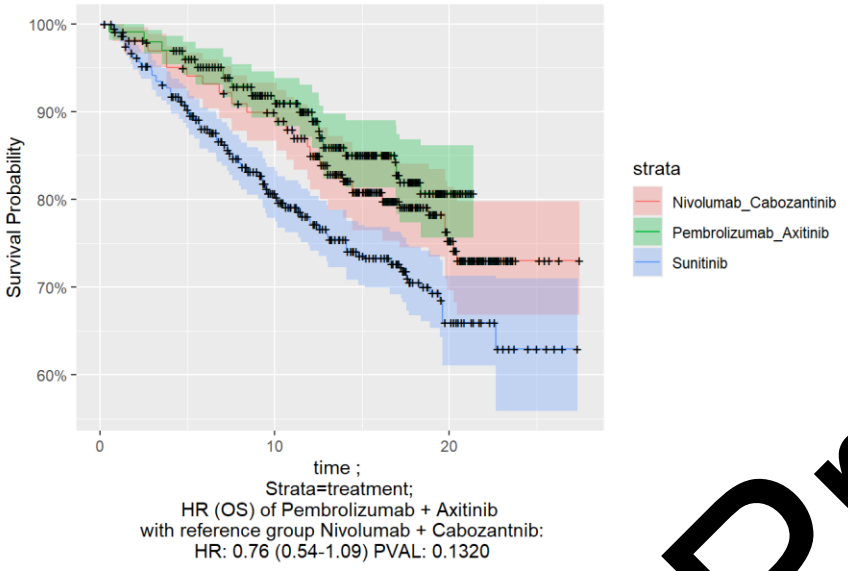


Figure 9: Survival Plot of the combined studies for OS endpoint

The Kaplan Meier plot and Hazard Ratio of Pembrolizumab plus Axitinib with respect to Nivolumab plus Cabozantinib is presented for Progression Free Survival in Figure 10.

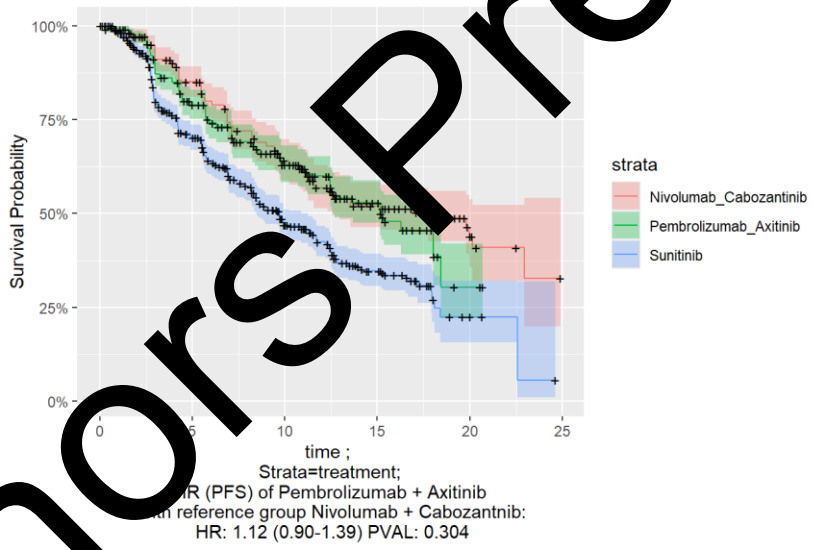


Figure 10: Survival Plot of the combined studies for PFS endpoint

The below plot in Figure 11 shows the close match in the survival curves obtained from Kaplan-Meier and the IDP method for overall survival of Sunitinib arm.

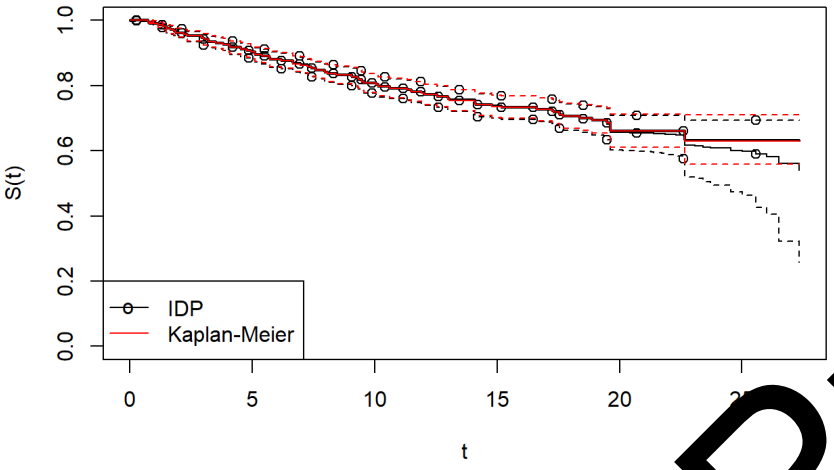


Figure 11: Comparative Survival Plot of Combined Sunitinib arm for OS endpoint by KM and IDP

The below plot in Figure 12 shows the close match in the survival curves obtained from Kaplan-Meier and the IDP method for progression free survival of Sunitinib arm.

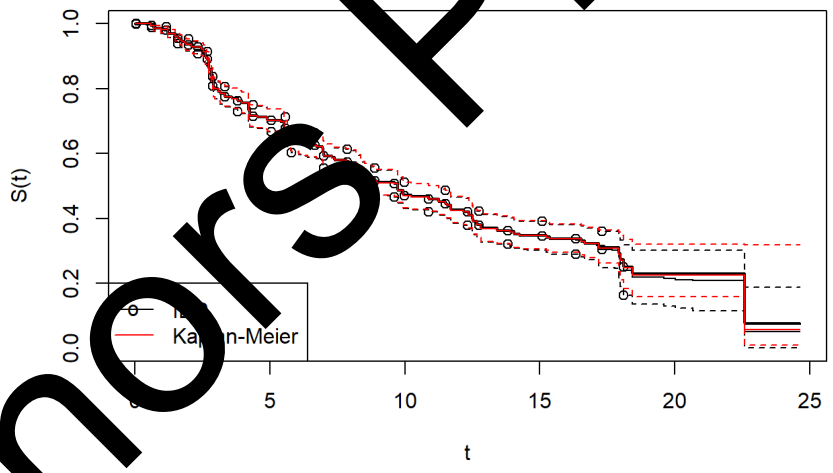


Figure 12: Comparative Survival Plot of Combined Sunitinib arm for PFS endpoint by KM and IDP

The survival curve of the combined data by treatment arm and by KM and IDP are shown below Figure 13 for overall survival

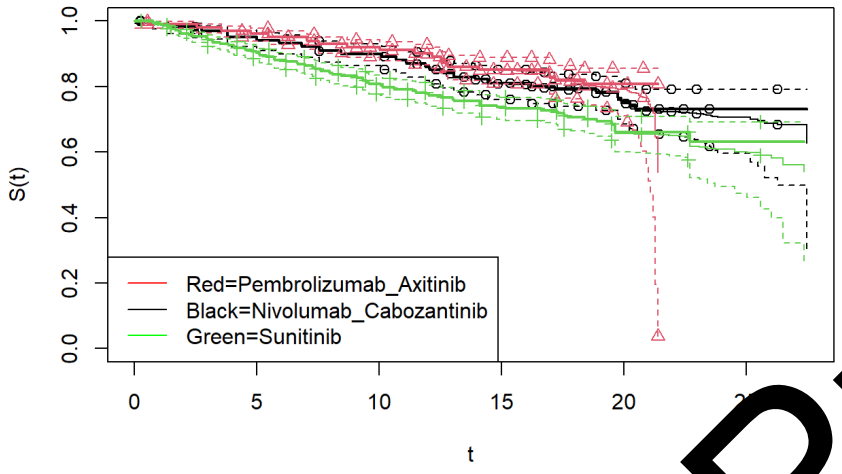


Figure 13: Comparative Survival Plot for OS endpoint by KM and IDP

The survival curve of the combined data by treatment arm and by KM and IDP are shown below Figure 14 for progression free survival.

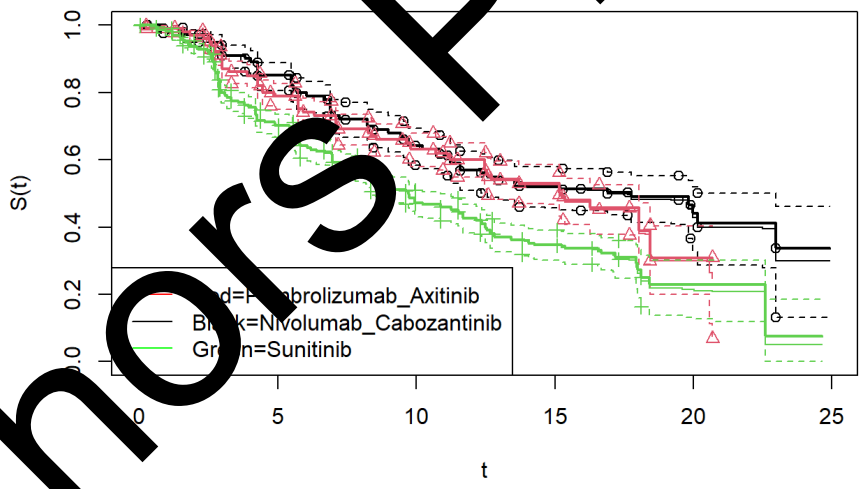


Figure 14: Comparative Survival Plot for PFS endpoint by KM and IDP

V. RESULTS AND DISCUSSION

The Sunitinib arm of the two studies did not show any significant statistical difference based on the log-rank test. Therefore, the data from the two studies were combined together with the Sunitinib considered as one overall reference group. The pembrolizumab-plus-axitinib and nivolumab-plus-cabozantinib were then compared once the link was established via the Sunitinib arm. In both the OS and PFS based analysis, there was no statistically significant difference between the 2 combination therapies. The results obtained from the Frequentist Cox-regression model and Bayesian non-parametric approach based on the DP showed similar trend. The use of near ignorance prior DP based survival analysis should be part of analysis along with cox-regression models. Unlike the MAIC based research paper that showed statistical

significance of one combination, use of all data from the pseudo-IPD does not show any difference in efficacy between the two combination therapies. Both combination therapies perform significantly better than Sunitinib arm in terms of efficacy. Thus, the cost of treatment, ICER and adverse event could be the main drivers to making a choice for the preferred treatment regimen.

It is important to note the limitations of generated pseudo IPD data and slight differences in estimates from digitized curves do get carried over to the aggregated estimates when data are combined. The stability of the common reference arm is crucial for the stability of indirect estimates. Hence a repository of important and common active treatment arms such as Sunitinib in specific therapeutic areas need to be created for reference and comparison. DP based method offers a relatively easy way of estimating results. There are alternate Frequentist and Bayesian methods and the appropriateness of the method need to be determined for specific scenarios.

VI. CONCLUSION

We conclude that the prior near-ignorance Dirichlet Process based NMA is a good choice compared to the cox-proportional Hazard Ratio based method as the need of proportionality assumption is no longer required. In the currently used dataset, the common reference arm data was homogeneous across the two studies. Hence, both the cox-regression and pseudo-IPD based methods produced similar results. In case of heterogeneity within the reference group, the results of pseudo-IPD based method would tend to be more accurate. More studies need to be done with non-proportional hazard-based data to gain better insights. Further work is needed to compare the method with the results based on NMA based on Dirichlet process mixture model with shrinkage priors.

6.1. R Packages Used

netmeta ; dplyr; tidyverse; rjags; IDPSurvival.

References

[1] Capitanio, U., Bensalah, K., Bex, A., Boorjian, S.A., Bray, F., Coleman, J., Gore, J.L., Sun, M., Wood, C., Russo, P.: Epidemiology of renal cell carcinoma. European urology 75(1), 74–84 (2019)

[2] Choueiri, T.K., Motzer, R.J.: Systemic therapy for metastatic renal-cell carcinoma. New England Journal of Medicine 376(4), 354–366 (2017)

[3] Li, S., Li, J., Peng, L., Li, Y., Wan, X.: Cost-effectiveness of nivolumab plus cabozantinib versus sunitinib as a first-line treatment for advanced renal cell carcinoma in the united states. Frontiers in Pharmacology 12, 736860 (2021)

[4] Ding, D., Hu, H., Shi, Y., She, L., Yao, L., Zhu, Y., Zeng, S., Shen, L., Huang, J.: Cost-effectiveness of pembrolizumab plus axitinib versus sunitinib as first-line therapy in advanced renal cell carcinoma in the us. The Oncologist 26(2), 290–297 (2021)

[5] McGregor, B.A., Geynisman, D.M., Burotto, M., Porta, C., Suarez Rodriguez, C., Bourlon, M.T., Barata, P.C., Gulati, S., Stwalley, B., Tejo, W., et al.: Efficacy outcomes of nivolumab+ cabozantinib versus pembrolizumab+ axitinib in patients with advanced renal cell carcinoma (aRCC): Matching-adjusted indirect comparison (MAIC). Wolters Kluwer Health (2021)

[6] Du, X., Li, M., Zhu, P., Wang, J., Hou, L., Li, J., Meng, H., Zhou, M., Zhu, C.: Comparison of the flexible parametric survival model and cox model in estimating markov transition probabilities using real-world data. PLoS One 13(8), 0200801 (2018)

[7] Kaplan, E.L., Meier, P.: Nonparametric estimation from incomplete observations. Journal of the American statistical association 53(282), 457–481 (1958)

[8] Schemper, M.: Cox analysis of survival data with non-proportional hazard functions. Journal of the Royal Statistical Society Series D: The Statistician 41(4), 455–465 (1992)

[9] Lee, E.T., Wang, J.: Statistical Methods for Survival Data Analysis vol. 476. John Wiley & Sons, New Jersey, NJ (2003)

[10] Apell´aniz, P.A., Parras, J., Zazo, S.: Savae: Leveraging the variational bayes autoencoder for survival analysis. arXiv preprint arXiv:2312.14651 (2023)

[11] Guyot, P., Ades, A., Ouwens, M.J., Welton, N.J.: Enhanced secondary analysis of survival data: reconstructing the data from published kaplan-meier survival curves. BMC medical research methodology 12, 1–13 (2012)

[12] Susarla, V., Van Ryzin, J.: Nonparametric bayesian estimation of survival curves from incomplete observations. Journal of the American Statistical Association 71(356), 897–902 (1976)

[13] Mangili, F., Benavoli, A., Campos, C.P., Zaffalon, M.: Reliable survival analysis based on the dirichlet process. Biometrical Journal 57(6), 1002–1019 (2015)

[14] Scharlau, R.: Metrical shellings of simplicial complexes. European Journal of Combinatorics 6(3), 265–269 (1985)

[15] Taboga, M.: Lectures on Probability Theory and Mathematical Statistics. CreateSpace Independent Publishing Platform, California, USA (2017)

[16] Ng, K.W., Tian, G.-L., Tang, M.-L.: Dirichlet and Related Distributions: Theory, Methods and Applications. John Wiley & Sons, New Jersey, NJ (2011)

[17] Lange, K.: Applications of the dirichlet distribution to forensic match probabilities. Genetica 96, 107–117 (1995)

[18] Frigyik, B.A., Kapila, A., Gupta, M.R.: Introduction to the dirichlet distribution and related processes. department of electrical engineering, university of washignton. Technical report, UWEETR-2010-0006 (2010)

[19] Ferguson, T.S.: Prior distributions on spaces of probability measures. The annals of statistics 2(4), 615–629 (1974)

[20] Leisen, F., Lijoi, A., Span´o, D.: A vector of dirichlet processes. Electronic Journal of Statistics 7, 62–90 (2013)

[21] Jara, A.: Theory and computations for the dirichlet process and related models: An overview. International Journal of Approximate Reasoning 81, 128–146 (2017)

[22] Hijazi, R.H., Jernigan, R.W.: Modelling compositional data using Dirichlet regression models. Journal of Applied Probability & Statistics 4(1), 77–91 (2009)

[23] Bucher, H.C., Guyatt, G.H., Griffith, L.E., Walter, S.D.: The results of direct and indirect treatment comparisons in meta-analysis of randomized controlled trials. Journal of clinical epidemiology 50(6), 683–691 (1997)