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A comparison of Frequentist and Bayesian network meta analysis with a case study from dental health data

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Abstract Network meta analysis is an extension of pair wise meta analysis where both direct as well as indirect treatment effects relative to a chosen reference treatment arm can be obtained from combined pool of studies as long as all the treatment arms are connected directly or indirectly via a network based on individual trials or studies. The aim of this network meta-analysis is to summarize and compare the results from Frequentist and Bayesian methods of the direct and indirect clinical evidence on the effectiveness of professionally applied topical fluorides in preventing dental root caries. Both the statistical approaches use different frameworks and each provides unique insights into the network of treatments approved for dental root caries. While the Frequentist approach provides the relative treatment effects along with corresponding confidence intervals compared to the usual care group, the Bayesian approach provides the relative treatment effects along with corresponding credible intervals. The full posterior distribution of treatment effects can be obtained using the Bayesian framework. Both approaches show similar direction of outcomes with subtle differences. A comparative analysis is presented and discussed using a case study using few topical fluoride-based treatment for dental caries. Various aspects of differences in approach as well as diagnostic checks and treatment ranking methods in both the frameworks are described. The netmeta package of R is used for the Frequentist approach while the geMTC package of R is used for Bayesian Analysis.

Keywords MA - Meta Analysis; NMA - Network Meta Analysis; SUCRA - Surface Under the Cumulative RAnking curve; MCMC - Markov Chain Monte Carlo; CrI - Credible Interval

AMS 2010 subject classifications 62P10, 62F15, 92B15

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1. Introduction

Network meta-analysis (NMA) is is a relatively novel approach that enables to estimate relative efficacy between treatments that may not have been compared directly, as long as they are interlinked within the network via a common direct arm ([1], [2], [3]). The NMA has advantages over pairwise meta analysis ([4]) one of which is that it incorporates direct and indirect comparisons ([5]).

NMA can be considered as a superset encompassing all individual pairwise comparisons done within the scope of a clinical trial with at least two treatment arms. Please note that there could be more than two treatment arms in individual studies. Figure 1 gives a general description of the relationship between NMA and pairwise comparison.

The initial steps towards conducting a NMA remain similar to the process of conducting a pairwise Meta Analysis.

The objective and inclusion/exclusion criteria need to be set based on the PRISMA guidelines ([6]) and we need to adhere to the PICOT rules where P refers to population or problem, I stands for intervention, C as a placeholder

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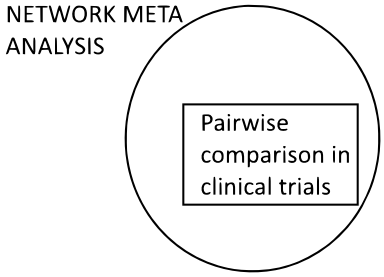

Figure 1. Network Meta Analysis with respect to pairwise comparison

for comparison group with O referring to the outcome endpoint and T indicating the time-frame of included study endpoint.

Any relevant study with treatment arms can be part of the NMA as long as they have a common connecting arm to another study treatment arm. For example, several studies with placebo as one of the treatment arms in each study can be part of the NMA since all other treatment arms are connected via the placebo arm. Similarly it could be based on active treatment reference arm. For example, in Renal cell cancer treatment, there are several combination therapy clinical trial results with respect to an active Sunitinib treatment reference arm. Therefore such studies can be potentially combined and different combination therapies can be compared indirectly with each other via a common connecting note that is the active Sunitinib reference arm. One should be cautious when treating Placebo of all studies as the same. When combining studies with placebo arm, ideally the studies should be from trials with similar start years. The placebo effect change can be checked by time and year. Sometimes placebo effects can be very different in individual studies.

Below Figure 2 is an example of an isolated study that fits the inclusion criteria for NMA but cannot be included as both its treatment arms do not have a match with the treatment arms in the network.

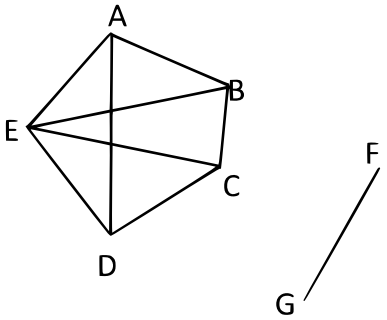

Figure 2. Isolated node disconnected from rest of network

Another issue is when combining active treatment arms, sometimes the route of administration has a differential effect on the efficacy estimates. Therefore, we suggest to use the treatment name as a combination of name of drug, dose level, route of administration and frequency of administration. Route of administration could be oral, intravenous, intramuscular etc. while the frequency is usually mentioned in terms of QD (every day/daily), BID (twice in day) etc.

The purpose of this study is to present a network meta-analysis of few topical fluoride based medical interventions to prevent dental root caries. Estimates available at the end of 2 years from start of intervention have been used as data for analysis from 3 of the 4 included study. Wallace study results however from a 48 month time frame was used as we could not get the 24 month time frame result in public domain.

Clinicians and patients often have to make a decision to choose from a range of alternate medication choices ([7]). For dental root caries too there are a plethora of approved drug options. The choice of the best treatment option becomes all the more difficult if there are no head-to-head trial data between any 2 drugs at a time from the

list of treatment options. NMA is an extension of the meta analyses that allows the simultaneous comparison of multiple agents against one another using both direct and indirect comparison as long as the studies or trials in the NMA are connected to each other with no isolated treatment([8])). Methodologies have and are evolving at a rapid pace. The end benefit of NMA is that they provide an overall ranking of all the networked treatment arms and also provide the relative effect size of each treatment against the usual-care group or standard reference.

Bayesian and Frequentist frameworks have evolved to perform the NMA. Several software such as OpenBUGS, WinBUGS, Stan, Stata and R based packages have evolved to perform NMA ([9, 10, 11]).

Network meta-analysis (NMA) is a synthesized and evolved version of traditional pairwise meta-analysis ([12, 13]) and the application of NMA has increased and evolved in recent years ([14, 15]). NMA is a value added tool in the repository of analysts, researchers and to those who take Medical decisions when facing alternate clinical scenarios which needs a comparative analysis of multiple alternative treatment regimens, as well as situations where both direct and indirect evidence data exists to address the research question ([16, 17]).

Methodology of NMA related research and analyses using NMA has evolved over the years, and its application has been augmented by the use of additional statistical tools, diagnostics and graphical output options as well as standardization of reporting guidance and tools for testing bias and strength of evidence ([18, 19, 7, 5]).

NMA analysis is broadly divided into two frameworks, the Frequentist and the Bayesian ([20])

In the Frequentist framework, the parameters are considered fixed and estimated from the available observed data at hand. Based on a priori threshold, the hypothesis can be tested and accepted. The results of the Frequentist framework provide us the estimates along with the appropriate confidence interval (Ci) values([21]).

The Bayesian framework is based on conditional probability and probabilistic distribution of the parameters taking into account both the observed likelihood based on available data and the priors that encapsulate additional information available outside of the study. The Markov Chain Monte Carlo (MCMC) simulations approach is used to model the data till the estimates converge well and stabilize to be used as posterior probability.

The Bayesian estimates are presented in the form of point estimate along with information about its corresponding credible interval (CrI) ([21, 22]).

Our results are based on the standardized mean difference relative to the usual care group (control group)

Zhang et-al ([23]) have presented results from a professionally applied treatment NMA using Frequentist framework in Stata with a fixed effect model due to instability of random effects model in their software though they acknowledged the presence of heterogeneity.

We have replicated the Frequentist work using netmeta package of R for the professionally applied treatments using data from 4 different trials. Random effect model in netmeta package of R was used for the Frequentist analysis. We have also done the analyses using a Bayesian framework using gemtc package of R. Random effects model was used and convergence was detected in model.

While the results from both the approaches point to the same direction and ranking of treatment is similar with the same treatment getting best rank in both, there are subtle differences. The input dataset of NMA based on individual Randomized Controlled Trials ensured quality input and helps in ascertaining relative treatment effects estimates among treatment groups which otherwise would not be possible in the absence of head-to-head trials.

Important checks are needed for assumptions such as transitivity and consistency. Transitivity means that the treatment comparisons should be ideally immune from effect modifiers. Consistency refers to the condition that direct and indirect comparison effects are similar. The issues of bias should be checked similar to the approach used in meta analysis.

2. Methods

The objective of the study is to compare the results from Frequentist and Bayesian frameworks of NMA. A previous study (Zhang et al) ([23]) did a Frequentist NMA on dental root caries separately for professionally applied drugs and for self-medication using STATA software. The average number of root caries were the endpoint estimates for NMA.

We checked the Pubmed, Clinicaltrial.gov and Medline for randomized clinical trials that had professionally applied treatment arms to treat dental root caries. Four studies from included are Wallace([24]), Tan ([25]), Zhang ([26]), Li ([27]) met the criteria with 6 different arms including the 'care as usual'/placebo arm.

The search strategy was as follows. For PUBMED, the search was based on: ("root[Title/Abstract]" AND ("caries[Title/Abstract]" OR "decay[Title/Abstract]" OR "carious[Title/Abstract])) AND ("fluoride[Title/Abstract]") AND ("prevention[Title/Abstract]"). There were 138 hits. For Cochrane library, the search was based on: ((ROOT AND (CARIES OR DECAY OR CARIOUS)) AND FLUORIDE AND PREVENTION). There were 2 hits. For Clinicaltrial.gov, the search was based on: (root AND (caries OR decay OR carious)) AND (fluoride) AND (prevention). There were 16 hits. FOR Medline PROQUEST, the search was based on: (root AND (caries OR decay OR carious)) AND (TOPICAL) AND (fluoride) AND (prevention) AND (OLDER) AND (ADULT) AND (RANDOMIZED) AND (CONTROLLED) AND (TRIAL). There were 304 hits from the scholarly journals filter. The research papers were extracted from the 4 databases as detailed above. Two independent reviewers screened the papers based on the title and abstract. The 29 filtered papers were reviewed and the final selection of 4 eligible papers was made.

The PRISMA flow diagram is provided below in Figure 3 for reference.

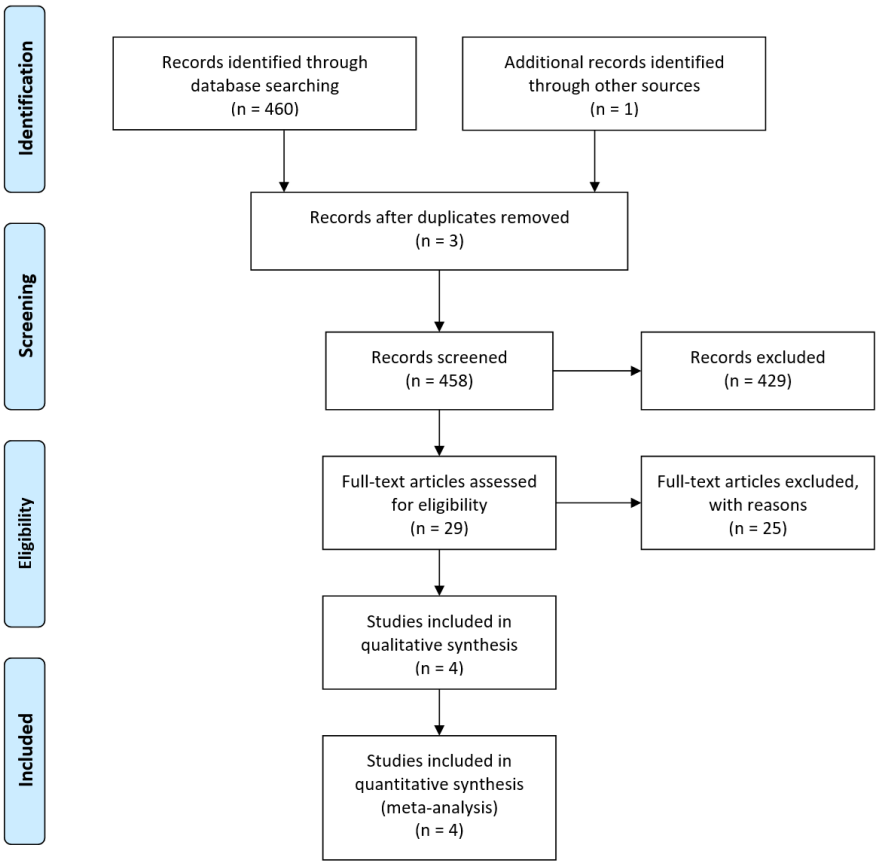

Figure 3. PRISMA 2009 Flowchart

Study	Age	Gender (Female percentage)
Li	72.1	78.3
Tan	78.8	76
Zhang	72.5	74.4
Wallace	60+	71 based on attrition rate by gender

Table 1. Covariate Mean estimates by Study

The Risk of Bias 2 (RoB 2) tool was used to assess the risk in the included studies. The Wallace study had some additional risk. All studies did suffer from missingness, but were assumed to be of low category. It is provided in Figure 4.

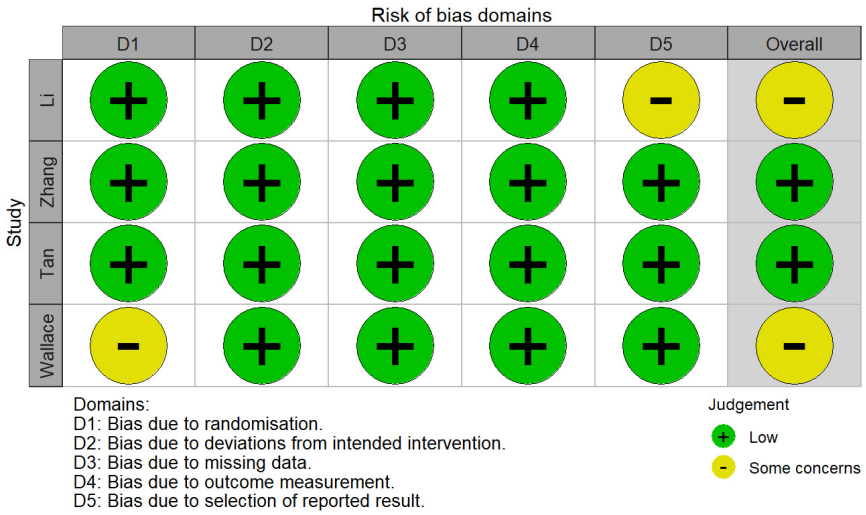

Figure 4. Risk of Bias based on (RoB2) tool

The terms Placebo, Control and 'Care as usual' are used interchangeably in the context of this study. The other 5 treatment arms in the study were: Sodium Diamine Fluoride (SDF), Sodium Diamine Fluoride with Potassium (SDFKI), Apf Gel(Apfgel), Sodium Fluoride, and Oral Health Education (OHE). OHE group included SDF as part of treatment.

The results at the end of 2 years of each study was used for the NMA. If result at 2 years was not available, the nearest next available time point post 2 years was used. There were potential confounders such as age and gender. The mean age and gender proportions for each of the studies are provided in Table 1. The estimates and standard errors of the endpoints used for NMA are provided in Table 2

The placebo estimates at year 4 for Wallace study were in the range of placebo effects for the other 3 studies. The follow-up in the Wallace study was every 6 months and no assessment of caries prior to month 48. Therefore, Wallace study is in main analysis. A sensitivity analysis is done excluding the Wallace study.

R v4.3.1 or above was used or the analysis. R netmeta package and R gemtc package were used for the Frequentist and Bayesian analysis respectively.

Study	Mean	standard error	N	Endpoint time
Li	1.1	0.16	80	24month
Tan	2	0.3	227	24month
Zhang	1.33	0.21	75	24month
Wallace	1.99	0.20	171	48month

Table 2. Placebo group new caries estimates for the 4 studies

2.1. Frequentist Estimates of NMA

The classical (Neyman—Pearson) statistical approach is popularly known by the term 'Frequentist' approach. This approach for statistical inference relies on the theory of large numbers and the repeat of experiments. This approach provides us the 'long-run frequency' estimates. The Frequentist approach considers the parameters to have one true effect size.

In R environment, the netmeta package is a popular package for conducting NMA using the Frequentist approach. Netmeta used a graph-theoretical approach for NMA based on a previous work in electrical network theory. A study by Rücker et al reported it as equivalent to the frequentist approach using weighted least squares regression ([28]).

In the frequentist framework, Rücker and Schwarzer developed a P-Score based approach as an equivalent of the Bayesian Surface area under the cumulative ranking curve (SUCRA) to rank the treatments based on a probability of each treatment being better than the other treatments in the network ([29]).

2.2. Bayesian Estimates of NMA

Bayesian inference represents a statistical methodology focuses on estimating specific parameters, such as a proportion or ratio, obtained from the population distribution based on the information contained in the included observed data. The Bayesian method for statistical inference therefore mimics the real-world approach for answering research questions, and it uses simulation to obtain the parameter estimates based on population distribution, instead of only relying on the sampling distribution which is the norm in the Frequentist approach. In Bayesian framework, the parameters are treated as random variables, allowing them to be characterized by probability distributions.

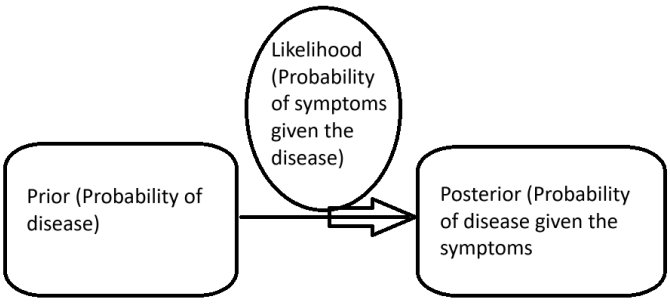

Figure 5. Bayesian approach

A notable feature of this approach is the interlinking of prior information with the included analysis data. In this framework, the prior as well as included data are expressed through family of distributions, which are referred to as prior distributions and distribution of likelihood, respectively, in Bayesian terminology. Figure 5 summarizes the Bayesian approach.

The prior distribution is integrated to the likelihood to refine existing information, leading to the posterior distribution, denoted as p('θ'/y). Here, 'θ' signifies the parameter of research outcome, while 'y' denotes the included data. The result obtained from a Bayesian analysis includes the posterior distribution, which can be characterized using descriptive statistics with the help of sampling techniques.

Credible Intervals (CrIs) are used in Bayesian statistics. They represent a range of plausible values for a parameter based on the observed data and prior beliefs. The credible level (e.g., 95 percent) indicates the probability that the true parameter lies falls inside the interval conditioned on the data and prior information. It can be interpreted as "There is a 95 percent probability that the true parameter falls within this interval."

The rjags is an interface between R and Just another Gibbs Sampler (JAGs). JAGs method is used for the Monte Carlo Markov Chain based sampling from posterior distribution.

Results of Frequentist and Bayesian network meta analysis using netmeta

The network plot in Figure 6 shows the way each treatment arm is linked to other treatment arms in direct and indirect manner. The thickness of the line joining any two arms increases with the increasing number of unique separate head-to-head trials.

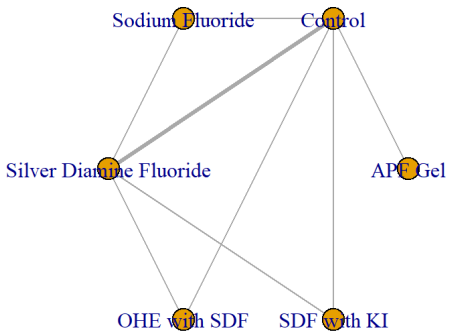

Figure 6. Network plot (netmeta)

The direct-indirect proportion per network is presented in Figure 7 below from netmeta output.

Eggers test was employed to detect any bias based on the funnel plot asymmetry. No major deviation was detected as shown in Figure 8. The treatment effects relative to control were used for the plot.

The transitivity assumption was checked in the random effects Frequentist method using the node splitting method. The direct versus indirect estimates were checked. The below plot Figure 9 shows that there are no major deviations noted in the direct versus indirect estimates except the Sodium Fluoride (Naf) versus Control. Only results of those treatment pairs are provided where both direct and indirect effects are estimable. For example APF gel versus SDF are not present as direct estimates are unavailable.

A meta-regression model was fit using the gemtc package with the estimates fitted against the co-variate with the 'risk of bias' (RoB) for each study in the input dataset. Wallace study had a higher risk of bias(1) as against 0 for the other three included studies.

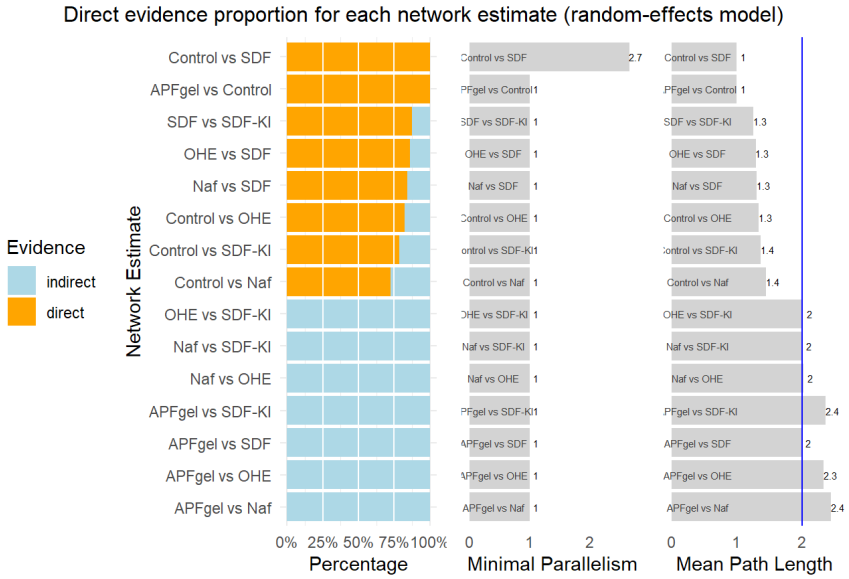

Figure 7. Direct evidence proportion for each network(Random effect) (netmeta)

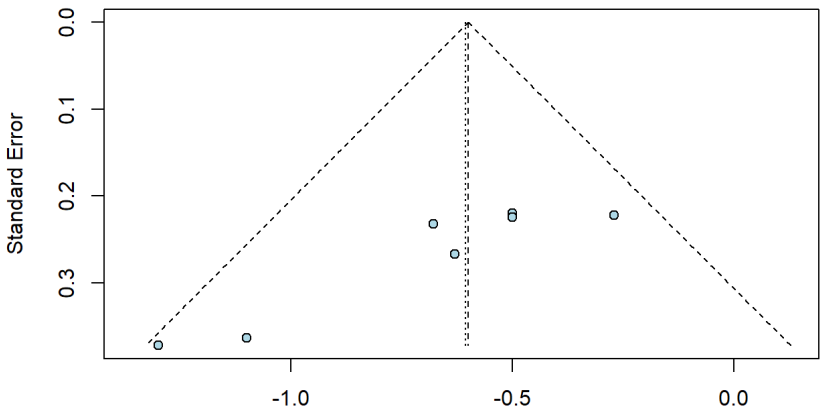

Figure 8. Egger's Test) on full data (4 studies data)

The result for the low-risk of bias estimates is provided in the below Figure 10. "Low Risk of Bias" and it visually compares the mean differences (with 95 percent credible intervals) of several treatments versus a control group. However, credible intervals for all treatments include zero, indicating no statistically significant difference at the 95 percent level. The widest interval is for APF Gel, suggesting more uncertainty in its effect estimate.

As part of sensitivity analysis, a separate model was fit excluding the data from Wallace study. The node splitting using the remaining 3 studies data in a random effects model showed a similar trend as obtained using the data from all 4 studies. Figure 11 shows the transitivity check on the random effects Netmeta based Frequentist model excluding Wallace study data.

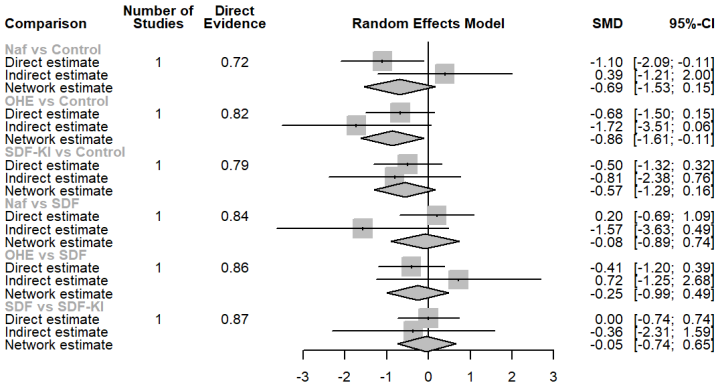

Figure 9. Transitivity check on the random effects Netmeta based Frequentist model) (netmeta)

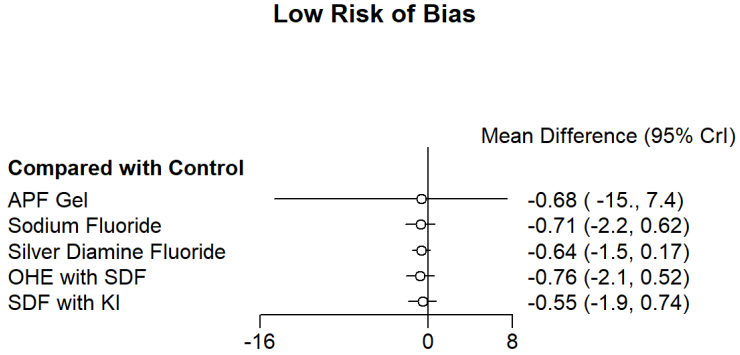

Figure 10. Low risk of bias from meta regression with study Risk of Bias as covariate)

The estimates of net splitting are shown below in Figure 12.

The forest plot (in Figure 13) obtained from the netmeta package of R illustrates that Oral Health Education (OHE) is the best performing intervention arm compared to placebo (usual care arm). The relative effect size along with the corresponding 95 percent Confidence Interval (CI) with respect to placebo is represented. After OHE, application of Apf gel and use of sodium fluoride were the next two best performing treatment options for preventing dental root caries.

The results from the Bayesian network meta analysis using gemtc package of R also indicates that OHE was the best performing treatment approach. However the estimates for SDF and Apf gel were slightly different from

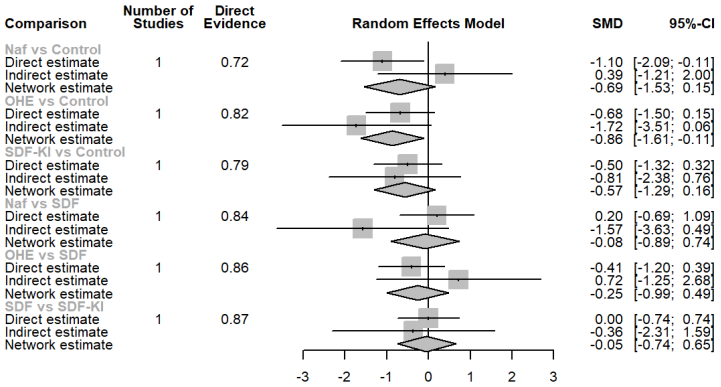

Figure 11. Transitivity check on the random effects Netmeta excluding Wallace study data

```
Random effects model:

       comparison k prop     nma  direct  indir.    Diff     z p-value
 APFgel vs Control 1 1.00 -0.6300 -0.6300       .       .     .       .
    APFgel vs Naf 0    0  0.0588       .  0.0588       .     .       .
    APFgel vs OHE 0    0  0.2318       .  0.2318       .     .       .
    APFgel vs SDF 0    0 -0.0182       . -0.0182       .     .       .
  APFgel vs SDF-KI 0    0 -0.0642       . -0.0642       .     .       .
   Naf vs Control 1 0.72 -0.6888 -1.1000  0.3922 -1.4922 -1.55  0.1212
   OHE vs Control 1 0.82 -0.8618 -0.6780 -1.7223  1.0443  1.04  0.2985
   SDF vs Control 3 1.00 -0.6118 -0.6118       .       .     .       .
 SDF-KI vs Control 1 0.79 -0.5658 -0.5000 -0.8085  0.3085  0.34  0.7327
       Naf vs OHE 0    0  0.1730       .  0.1730       .     .       .
       Naf vs SDF 1 0.84 -0.0770  0.2000 -1.5720  1.7720  1.55  0.1212
    Naf vs SDF-KI 0    0 -0.1231       . -0.1231       .     .       .
       OHE vs SDF 1 0.86 -0.2500 -0.4080  0.7173 -1.1253 -1.04  0.2985
    OHE vs SDF-KI 0    0 -0.2960       . -0.2960       .     .       .
    SDF vs SDF-KI 1 0.87 -0.0461  0.0000 -0.3636  0.3636  0.34  0.7327

Legend:
 comparison - Treatment comparison
 k          - Number of studies providing direct evidence
 prop       - Direct evidence proportion
 nma        - Estimated treatment effect (SMD) in network meta-analysis
 direct     - Estimated treatment effect (SMD) derived from direct evidence
 indir.     - Estimated treatment effect (SMD) derived from indirect evidence
 Diff       - Difference between direct and indirect treatment estimates
 z          - z-value of test for disagreement (direct versus indirect)
 p-value    - p-value of test for disagreement (direct versus indirect)
```

Figure 12. Transitivity check estimates using all 4 studies) (netmeta)

that obtained in the Frequentist framework. The estimates and Credible intervals are provided. Please note that a weakly informative prior has been set using the values 0 to 2 for a uniform prior for standard deviation of random effects (heterogeneity in treatment effects across studies). The results are presented in Figure 14.

The Monte Carlo Markov Chain method was used to sample from the posterior distribution of the estimates from Bayesian analyses. For chains were used. 5000 burn-in samples were used and 10000000 samples were generated with a thin of 50 which translated to an effective sample size (ESS) of 200000. The Potential Scale Reduction

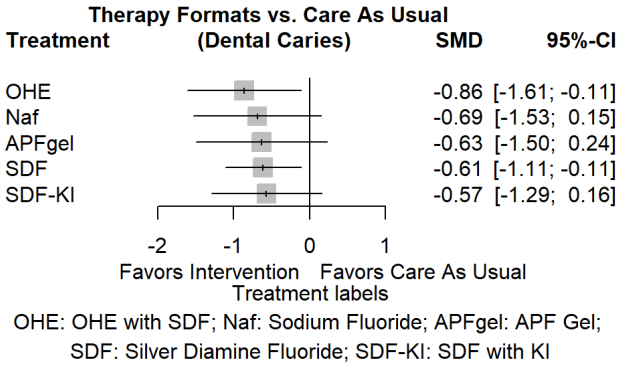

Figure 13. Forest plot (netmeta)

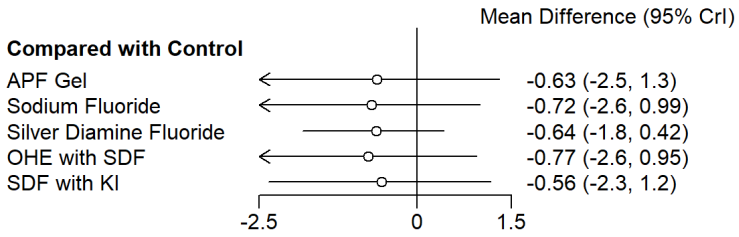

Figure 14. Forest plot (gemtc)

Factor (PSRF) for the overall model was nearly 1 (1.000016 approximately). The PSRF is a ratio of within chain variation to that of the between chains variation, and their trend over time. To ascertain if convergence is met, the PRSF should ultimately shrink down to zero and at least below 1.05.

Gelman-Rubin diagnostics were checked to assess convergence.

The figure 14 shows that the Oral health education which included SDF as one of its components performed best relative to the control group. Sodium Flouride came in at the second spot.

The diagnostic plots in Figure 5 seemed to suggest that convergence was well met as per the traceplots. The results of control group are presented. All other treatment arm traceplots were checked and in each case convergence was met. Figure 15 and Figure 16 together show the convergence diagnostics.

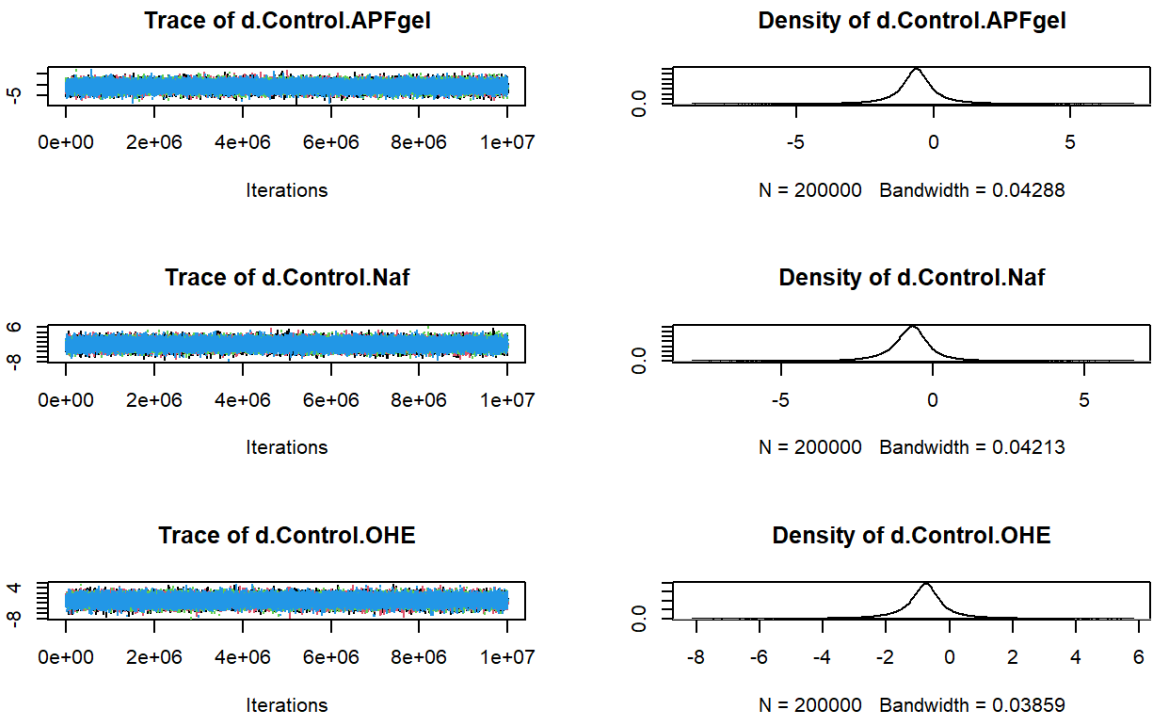

Figure 15. convergence (gemtc) part1

The rankogram plot is provided in Figure 17. Since the first bar which is an indicator of the first rank, is highest in OHE, it points to OHE being the best option.

The Bayesian analysis also provided the SUCRA ranking to treatment arms. As per the SUCRA plot the OHE gives the best protection among the treatments, followed by Sodium Fluoride. The results are presented in Figure 18. The SUCRA rankings are sensitive to the choice of endpoint used.

3. Key Differences in the 2 Frameworks and Result Interpretation

There are some key differences in the way results are interpreted using the classical Frequentist method and those using the Bayesian framework. In the Frequentist framework, the results are akin to stable estimates based on numerous repeated samplings or series of experiments. The p-value or confidence intervals signal whether the results are significant or otherwise. In the Bayesian framework, the estimates are based on probabilistic sampling from the posterior distributions obtained from a combination of prior and likelihood. NMA using Bayesian approach tend to take care of hierarchical data structures better. The framework impacts the conclusions, and have a critical bearing when guiding the clinical decision-making process. It is important to note the limitations and assumptions underneath each of the framework.

The results from both the frameworks were in close agreement in terms of estimates and ranking. The Bayesian Credible Intervals however failed to show difference of any treatment group compared to the control group.

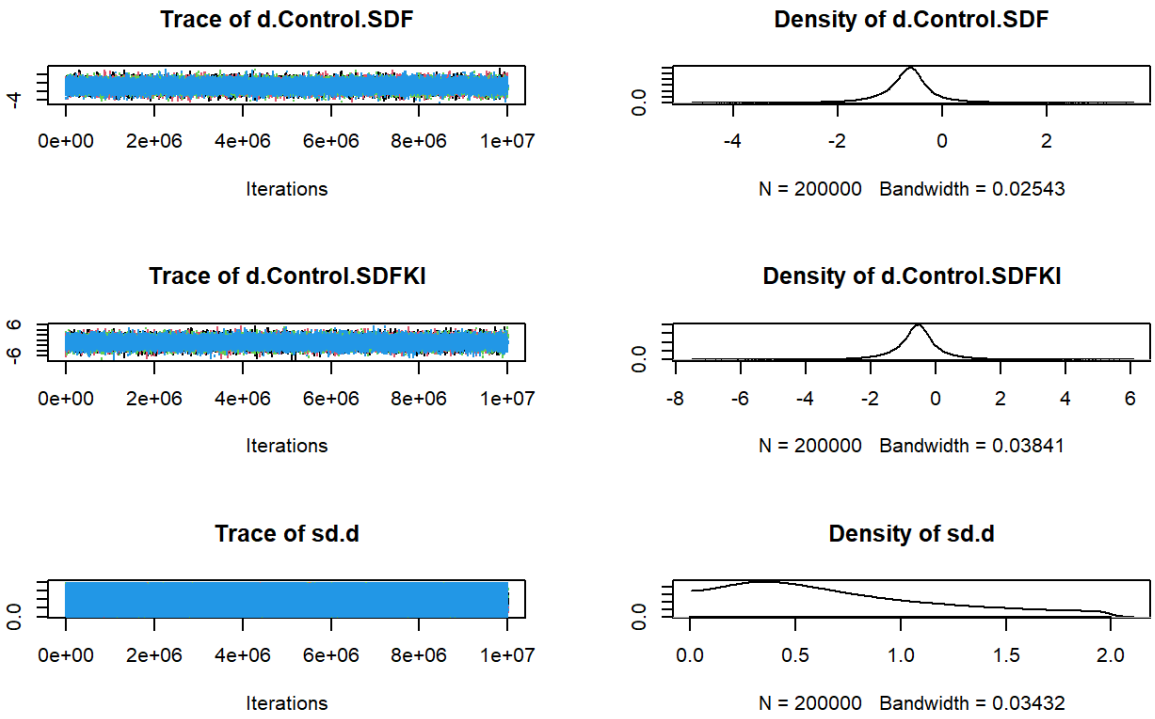

Figure 16. convergence (gemtc) part2

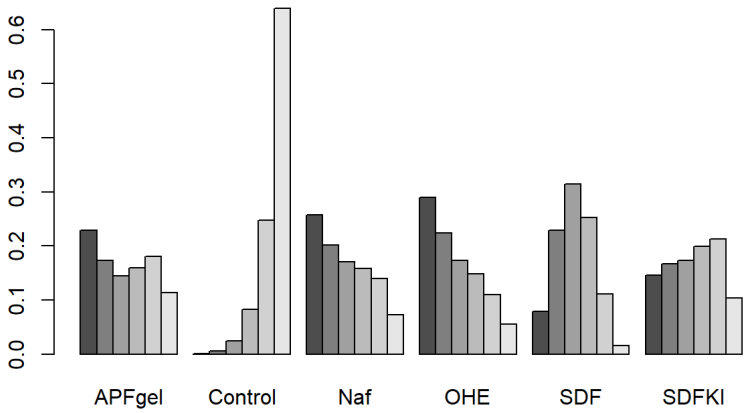

Figure 17. rankogram (gemtc)

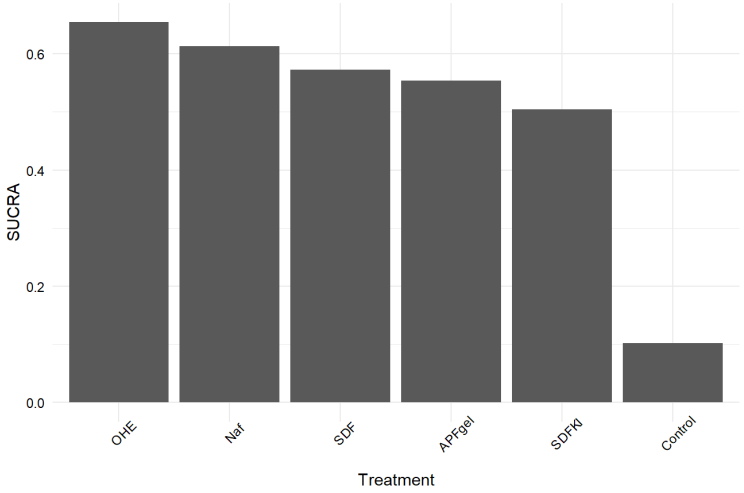

Figure 18. convergence (gemtc)

3.1. Sensitivity Analysis

Since there are some concerns regarding the bias involving the Wallace study, a sensitivity analysis was conducted using both the frameworks with data from the remaining 3 studies and excluding the data from the Wallace study. The Apf gel treatment arm is therefore no longer part of the sensitivity analysis.

The forest plot of the Frequentist random effects model for the sensitivity analysis (excluding Wallace study data) is provided in the Figure 19.

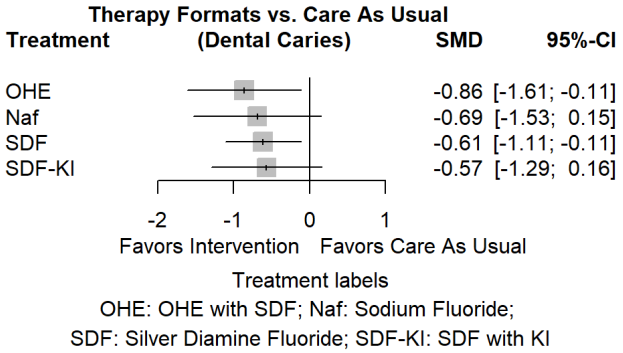

Figure 19. Netmeta sensitivity analysis forest plot (excluding Wallace study data)

Similarly the forest plot of the sensitivity analysis based on Bayesian NMA using gemtc package shows that the estimates of the remaining treatment arms were not impacted by the removal of the Wallace study data. The forest plot is shown in Figure 20.

The additional of Wallace study therefore adds the APF gel treatment arm to the list of competing treatment arms.

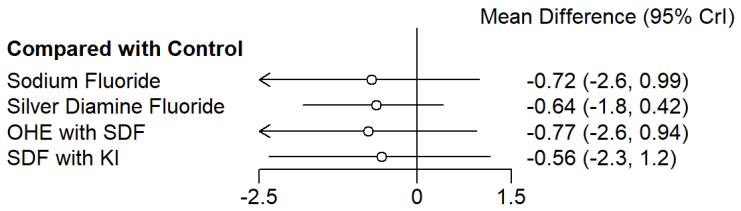

Figure 20. gemtc sensitivity analysis forest plot (excluding Wallace study data)

4. Discussion

NMA as a step wise additive tool for evidence synthesis in medical interventions is an established fact ([14]). While NMA has been applied in the dental root caries treatment space, a comparison of Frequentist and Bayesian frameworks based analysis has not been reported to the best of our knowledge.

While the results from both the Frequentist and Bayesian frameworks points towards the same direction, both highlight different aspects in terms of interpretation. The Bayesian approach based estimates are a closer approximation from population using direct sampling from posterior distribution, compared to the hypothetical approach that the Frequentist method takes. The conditional nature of the Bayesian framework, make it a preferred choice. However, the small number of 4 studies used in the analysis is a limitation and addition of new studies could impact the estimates.

The 95 percent CI from Frequentist approach means that if we repeat the analysis 100 times, 95 percent of the times the CI will contain the true effect size. Clinicians actually require a 90 or 95 percent confidence around the estimates. For example researchers and clinicians require that there be a 90 percent probability that the real effect estimate lies within the 90 percent CI and this is what the Bayesian Credible intervals provide. The Bayesian Credible intervals are therefore able to solve this requirement.

Frequentist CIs inform how estimates fluctuate across samples. In contrast the Bayesian CrIs inform the probability of containing a true parameter based on prior and observed data. Therefore, while the estimates from both frameworks are expected to be similar, the interval ranges could be vastly different as they are not equivalent and need to be interpreted differently.

Since there are 4 studies in this NMA, the Bayesian estimates should be used to augment the findings of the Frequentist estimates. The non-significant difference relative to 'care as usual' group in Bayesian should be further investigated in terms of the heterogeneity of 'care as usual' placebo effect across the studies. The low number of studies could be a potential limitation.

The Tan *et al* study had average number of 14.3 ± 6.5 teeth at baseline. The Wallace study did not specify baseline age and gender proportion. The gender percentage values were derived from attrition rates of first year. The study mentioned 60+ age group as target population.

In future, when results are available for trials such as for clinical trial registered with identifier number NCT05765058, the NMA results could be more meaningful.

As new randomized controlled trials with similar inclusion/exclusion are available, the analysis should be repeated to check for the stability of results currently obtained in this study.

NMA using the Bayesian framework based on the probabilistic nature of the queries tackled by NMA tend to be based on conditional probabilities, and therefore it works better with the hierarchical data structures. Further, such comparisons need to be done with more complicated data networks to better understand the methodological aspects.

There is a greater focus on clinically significant differences rather than statistical difference between treatment arms. Minimum clinically important differences (MCID) based on efficacy and patient satisfaction are yet to be established in dental care. Once MCID levels are established in this space, the NMA needs to be conducted with respect to the clinically important threshold.

5. Conclusion

Through our results of the classical Frequentist and the Bayesian methods, we have shown that both methods tend to convey the similar results. The treatment rankings based on the SUCRA needs to be interpreted in the context of the defined endpoint and its sensitivity in terms of other endpoints and cut-off definitions needs to be factored in. Our dataset is comparatively small with only 4 studies included. As the data increases in volume, we expect the Bayesian method to perform better. Further work with larger number of included studies and hierarchical structure in terms of multiple timepoints are needed in this direction.

6. R Packages Used

netmeta ([30]); gemtc([31]); dplyr; tidyverse; rjags

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