Possibilistic Approach for Meta-analysis

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Abstract. Meta-analyses offer interesting tools for combining the results of studies carried out by several authors on the strength of the observed effect of one variable on another, also called the effect size. The models proposed for the meta-analysis are within the statistical framework, which makes it possible to make hypotheses on the parametric probability laws related to the effect size variable. However, probability theory shows its limits for combining information from heterogeneous sources. In the absence of the assumption of homogeneity, the aggregation by a weighted average of the effect sizes, adopted in the meta-analyses to obtain the final effect size, does not seem to reflect the information provided by most sources. In this article, we propose a meta-analysis that takes advantage of possibility theory techniques to combine incomplete information from heterogeneous sources. The resulted possibility distribution allows to distinguish between plausible and less plausible values for the effect size of a treatment, for example, given trials performed by different authors. The illustration of the proposed possibilistic meta-analysis concerns the "post-COVID-syndrome". More precisely, the illustration focus on the prevalence of Fatigue symptom. The article shows that it is far from reality to consider the assumption of homogeneity for such data. Instead, group of coherent studies are identified using maximum coherent subsets. The results considering the two approaches are presented.

Keywords: Meta-analysis · Merging information · Possibility theory · Post-COVID · maximum coherent subsets.

1 Introduction

Meta-analysis [20] is a statistical approach which consists of combining the empirical results of studies carried out independently and according to certain criteria, i.e. according to a reproducible protocol, on the same clinical question to make a statistical synthesis [29]. Synthesis consists of producing an aggregate estimate closest to the unknown common truth. It has been applied most often to estimate the effect of a treatment following several randomized clinical trials [22] according to certain hypotheses [42] [41] but also to *incidence*, *prevalence*, or the best treatment for an epidemic. In practice, meta-analyses are conducted on a list of articles and studies that represent the state of knowledge on a specific research question or problem [29]. The strength of meta-analysis, and at

the same time its weakness, is that it allows the increase in the number of trials, compared to separate studies, and therefore to draw an overall conclusion. The object of study is essentially the effect size which is a measure of the strength of the observed effect of one variable on another [27]. The most common effect sizes are the standardized difference between two means, the odds ratio which compares the probability of an event in two groups, and the proportion or prevalence of a an observed variable. Despite the efforts made to approximate the necessary hypotheses on the studies that make up a meta-analysis, unfortunately there still remain various methodological problems. Therefore Meta-analysis, in our opinion, can be criticized for two main reasons: The first concerns adoption of the statistical approach based on probability theory for the representation of uncertainty and whose hypothesis of homogeneity of the tests is questionable. Indeed, probability theory shows its limits for combining information from heterogeneous sources. The second criticism concerns the choice of aggregation by weighted average of the effect sizes of heterogeneous studies. Indeed, in the absence of an assumption of homogeneity, the aggregation by a weighted average operator of effect sizes, adopted in meta-analyses to obtain the final effect size, does not seem to reflect the information provided by most of sources. Recently [25], work has been carried out to propose a meta-analysis that takes advantage of possibility theory techniques to combine incomplete information from heterogeneous sources in the case of odds ratio effect size. The result is to distinguish between plausible and less plausible values for the effect size of a treatment, for example, given trials provided by different authors. For example, if there are two different groups of patients undergoing studies of the effect of a treatment in two randomized controlled trials reporting conflicting results, the mean calculated by the meta-analysis is not representative of either of the two groups. Aggregation is much more suitable when seeking a compromise between the preferences of a decision-maker on several criteria or of several decision-makers on the same criterion. However, the objective of a meta-analysis is to find an overall estimate, from studies, which is as close as possible to the unknown true effect size. Thus, the combination of information by logical operators seems to us more appropriate for seeking the common truth within information coming from different studies [18]. In this sense, this article, as an exploratory work, proposes to explore the possibility theory tools of representations and logical combinations of incomplete information from heterogeneous sources taking into account their reliability. The illustration of the proposed possibilistic meta-analysis concerns the "post-COVID-syndrome". "Post-COVID syndrome" is known as a name commonly given to the various long-term symptoms caused by the COVID-19 disease [31]. It is characterized as a complex state of health, i.e., long-term negative effects, in patients who have just recovered from COVID-19 [31]. More precisely, the illustration focus on the symptom of "Fatigue" which is a persisting symptom characterizing the "post-COVID-syndrome" with the highest prevalence percentage in the most statistical studies and affects daily life of patients.

2 Backgrounds

2.1 Elementary Concepts of Meta-Analysis

2.1.1 The fixed and random models Let us consider K randomized trials. In a meta-analysis, the fixed effects model considers the assumption of homogeneity of treatment effects across all K studies. In other words, for each study k, the estimated treatment effect $\hat{\theta}_k$ has a distribution with common mean θ and individual variance v_k for $k = 1, \ldots, K$. The mean θ is then estimated, in the case of the fixed model, as a weighted average of the effect estimates in each study, that is, $\hat{\theta} = \sum_{k=1}^{K} w_k \cdot \hat{\theta}_k / \sum_{k=1}^{K} w_k$, where w_k is the weight given to study k, generally considered to be the inverse of the variance v_k [43]. If furthermore, $\hat{\theta}$ can be considered as following a normal distribution, for example this is the case when each $\hat{\theta}_k$ approximately follows a normal distribution. A confidence interval for θ at level $100 \cdot (1-\alpha)\%$ can then be calculated as follows [13]: $IC_\alpha(\theta) = \hat{\theta} \pm \mathbf{z}_{1-\frac{\alpha}{2}} \sqrt{var(\hat{\theta})}$, where $var(\hat{\theta}) = 1/\sum_{k=1}^{K} w_k$ and $\mathbf{z}_{1-\frac{\alpha}{2}}$ is the quantile of order $1-\frac{\alpha}{2}$ which comes from the tables of the reduced and centered normal distribution. The mean estimate and the confidence interval of the formula also hold in the case of the random effects model [13] where a heterogeneity of treatment effects between studies is incorporate into the estimation by including a between-study variance component σ_B^2, where heterogeneity is restricted to a particular form. Indeed, for each study k we consider $\hat{\theta}_k \sim \mathcal{N}(\theta_k, v_k)$ where $\theta_k \sim \mathcal{N}(\theta, \sigma_B^2)$. It is almost as if we consider that each trial estimates a slightly different effect, and that this effect varies with different entry criteria, i.e., different treatment protocols, different environmental and genetic factors etc. in patients from different trials. The mean estimate of the treatment effect is again obtained with weights adjusted to incorporate σ_B^2, i.e. $w_k^* = \frac{1}{(v_k+\sigma_B^2)}$ [13]. If the assumption of homogeneity of treatment effects across all K studies is no longer verified, the challenge associated with the random effects model is then the estimation of the variance σ_B^2 [13].

2.1.2 The three levels meta-analysis model In addition, a third level of variance can be introduced to model the membership of certain patients in clusters. This is the case in social and medical domain analysis. For example, if we collect data on hospitalized patients from different hospitals in a state. The hospitals are sampled from the population of total hospitals in this state in a first level. The second level of sampling are the selected patients from each chosen hospital. Thus, the patients could be grouped according to the hospitals they were hospitalized. This way of conducting statistical studies could induce a dependence in results. In fact, two patients from the same hospital are, in general more similar than two patients from different hospitals. This fact is caused by the effect of the hospital. Multilevel meta-analysis models was introduced to take in account such dependences [21] [23]. The three levels meta-analysis model is

organised as follows:
The first level of the model: $\hat{\theta}_{kK_j} \sim \mathcal{N}(\theta_{kK_j}, \epsilon_{kK_j})$,
the second level of the model: $\theta_{kK_j} \sim \mathcal{N}(\theta_{K_j}, \zeta_{(2)kK_j})$,
the second level of the model: $\theta_{K_j} \sim \mathcal{N}(\theta, \zeta_{(3)K_j})$,
where some studies k belongs to the cluster K_j, parameter θ_{K_j} is the effect size of the cluster K_j, θ is the true effect size of the population, $\zeta_{(2)kK_j}$ characterizes the within-cluster K_j heterogeneity on level 2 and $\zeta_{(3)K_j}$ represents the between cluster heterogeneity.

2.1.3 The case of prevalence (or proportion) Meta-analysis of prevalence is often used in epidemiology research. Conventional meta-analyses proceed in two steps: 1) transform the proportion of each study, then 2) perform a meta-analysis on the transformed scale. Let us consider a meta-analysis containing K studies, each reporting event frequency e_k with sample size n_k $(k = 1, \ldots, K)$. The proportion of study events k is estimated as:

$$\hat{p}_k = \frac{e_k}{n_k}. \tag{1}$$

Its corresponding *logit* transformation is as follows:

$$g(\hat{p}_k) = \log\left[\frac{\hat{p}_k}{1-\hat{p}_k}\right], \tag{2}$$

with

$$\sigma(g(\hat{p}_k)) = \sqrt{\frac{1}{e_k} + \frac{1}{n_k - e_k}}; \tag{3}$$

A confidence interval of $100 \cdot (1-\alpha)\%$ for $\hat{p}_k$ is defined as follows:

$$IC_\alpha(g(\hat{p}_k)) = g(\hat{p}_k) \pm z_{1-\frac{\alpha}{2}} \cdot \sigma(g(\hat{p}_k)). \tag{4}$$

Meta-analyses of proportions are often very heterogeneous and are therefore often carried out using the random effects model.

2.2 Possibility theory

2.2.1 Information representation Possibility theory is a framework for representing uncertainty and imprecision to distinguish between plausible and less plausible values for a parameter or variable of interest [15] [19]. More precisely, let Θ be a closed and bounded real interval containing the true unknown value θ^* of a quantity of interest. A possibility distribution defined on Θ, $\pi_{\theta^*} : \Theta \to [0, 1]$, is a real function such that: π_{θ^*} associates to each element $\theta \in \Theta$ a degree of possibility $\pi_{\theta^*}(\theta)$ to be the true value θ^*. Thus, π_{θ^*} quantifies how more or less plausible a value of Θ is to be θ^*. We assume that there exists at least one value $\theta \in \Theta$ such that $\pi_{\theta^*}(\theta) = 1$ because it is certain that the true value θ^* is located in Θ. When for two different values θ_1 and θ_2 of Θ, $\pi_{\theta^*}(\theta_1) > \pi_{\theta^*}(\theta_2)$ this means that θ_1 is considered more plausible than θ_2. It is certain that θ^* does

not take a value $\theta \in \Theta$ if $\pi_{\theta^*}(\theta) = 0$. From π_{θ^*}, the possibility measure, denoted Π and the necessity measure, denoted N, are defined for any event $A \subseteq \Theta$, $\Pi(A) = \sup_{\theta \in A} \pi_{\theta^*}(\theta)$, $N(A) = 1 - \Pi(A^c)$, where A^c represents the complement of A in Θ. Moreover, the possibility distribution π_{θ^*} can represent a family of finitely numbered nested confidence subsets $A_1 \subset A_2 \subset \cdots \subset A_m$ where each A_i is attached to a positive confidence level λ_i such that $\lambda_i = N(A_i)$ [17]. The distribution representing these subsets, respecting the principle of minimal commitment, is written [18], $\forall \theta \in \Theta$,

$$\pi_{\theta^*}(\theta) = \min_{i \in \{1,\ldots,m\}} \max(\mu_{A_i}(\theta), 1 - \lambda_i), \tag{5}$$

where μ_{A_i} is the support characteristic function of A_i. The authors of [37] suggest using three intervals with predefined confidence levels: A_1 with $\lambda_1 = 0.05$, A_2 with $\lambda_2 = 0.5$, A_3 with $\lambda_3 = 0.95$ in addition to A_4 (with $\lambda_4 = 1$) which is always Θ. Furthermore, if the degree of certainty that a given source is reliable is known, say w, then it is possible to take this information into account by weakening a possibility distribution π into $\pi' = max(\pi, 1-w)$. If $w = 1$ (trusted source), then $\pi' = \pi$ and if $w = 0$ (untrusted source), then $\pi' = 1$ (vacuous distributions).

2.2.2 Combining possibility distributions [18] The possibilistic approach allows the combination of imprecise information from heterogeneous sources. Its main advantages over classical theories are: the fidelity of the representation of information, it does not need *a priori* knowledge, and the availability of a variety of combination methods whose choice depends on the reliability of the experts or sources and the level of conflicts between provided opinions or information [18]. Logical combinations such as conjunctive combinations denoted $\pi_\wedge$ or π_*, which is applied when all sources are reliable, and disjunctive combinations, denoted $\pi_\vee$, which deal with the case of unreliable sources hidden in a group of other reliable sources, constitute the main combinations in possibility theory [18]. In the presence of conflicts and/or unreliable sources, weighted logical combinations can be considered. Conjunctive combinations make sense if all π_k overlap significantly, i.e. $\exists \theta$, $\forall k$, $\pi_\wedge(\theta) = 1$, expressing that there is at least one value of Θ that all sources consider to be entirely possible [18]. However, in case of conflict, we can normalize $\pi_\wedge$ while keeping track of a partial conflict, the following normalized and weakened conjunctive combination rule has been proposed [18] [16] : $\forall \theta \in \Theta$,

$$\pi_{AD}(\theta) = \max(\frac{\pi_\wedge(\theta)}{h_\wedge}, \min(\pi_\vee(\theta), 1 - h_\wedge)) \tag{6}$$

where $h_\wedge = \sup_{\theta \in \Theta} \min_{k \in \{1,\ldots,K\}} \pi_k(\theta)$ is a consistency index. The combination rule in Equation (6) is a multi-source extension of the one defined in [16] for two sources. This extension is suggested with cautiousness in [16]. Indeed, it may not be effective if the sources are sparse because the consistency index will be zero and it is the non-informative disjunctive combination which will be the result.

3 The Possibilistic Approach of Meta-analysis

Our approach is based on the fact that in the case of meta-analysis, where we seek the true value of the effect size by combining the results of several trials, we are closer to the hypothesis of several different sensors which are used to measure the same quantity as the hypothesis of several measurements of this same quantity by the same sensor, as the result of a random experiment, which would justify the application of statistical tools. Thus, despite all efforts to make them homogeneous, heterogeneity exists between trials and it cannot be simplified by a random effect model. The three level meta analysis could be the adequate candidate model in case of cluster trials but the intra-cluster homogeneity is not guaranteed, e.g. trials concerning "post-covid syndrom" (see the illustration in Section 4). Consequently, the estimate using the mean, i.e. the data to be merged can be interpreted as a standard statistic, is not only inadequate in certain cases but it can, in most cases, be far from the estimates provided by each of the sources on the true desired value of the effect size. In general, we can consider the information provided by a trial as an expertise of the authors of the article from which it comes and as such, this information may be contradictory and/or in conflict with the information provided by other sources. In addition, these source may be more or less reliable depending on the date of the study, the size of the sample used, and other subjective elements of interest. As an alternative to the statistical approach to deal with this problem, possibility theory will seek to determine which values are plausible and which are less plausible based on values on which most sources agree. In this way, it offers a conservative response that fits the available data. The proposed approach is then organized as follows. Consider K trials testing the effects of a new drug or the prevalence of a symptom. In each trial, the treatment effect size is estimated and confidence intervals can be calculated.

- Each source k, e.g., provides a family of four nested confidence intervals A_1^k, A_2^k, A_3^k and A_4^k. In this case, the intervals are calculated according to the formula (4). The four intervals correspond to the confidence level 0.05, 0.5, 0.95 and 1. Note that, through the calculation of these intervals, we assume the statistical hypothesis within each single trials.
- The information provided by the source k is therefore represented by a possibility distribution π_k calculated from the confidence intervals according to the formula (5).
- If the information on the reliability of each source is known, each distribution π_k is discounted, i.e weighting the information regarding its reliability.
- Finally, the sources are combined according to the general formula (6). Indeed, it seems to us that this combination is adequate because there is no reason to doubt about the truth of the information provided by the sources.

In case of heterogeneous sources it is frequent to fall in the situation where some group of data conflict. In this case, sources should be separated depending on their coherence. In the case of classical three level meta-analysis clusters are considered representing common characteristics between sources like as the

same hospital, the same country, etc. However as it is the case in "post-covid syndrom" incoherence may also exist within clusters. In this situation, the maximum coherent subsets technique allows to determine the overlapping sources which are considered as coherent in the sense that they agree for some values to be plausible for the true unknown value of the effect size. The maximal coherent subsets (MCS) is a fusion technique for conflicting information that guaranties gaining the maximum of informativeness while any source is neglected. It consists of applying a conjunctive operator inside each non-conflicting subset of sources, and then to use a disjunctive operator between the partial results [36]. In the proposed approach, it concerns computing MCS of intervals [4], which is less computationally intensive, and more precisely the studies' confidence intervals at 95% level. More sophisticated merging computes MCS of intervals at different confidence levels [14].

4 Illustration

Fatigue is the most persistent and principal symptom that affects daily life of "post-COVID syndrome" patients. Several recent studies that deal with estimation of "post-COVID syndrome" symptoms prevalence show highest prevalence of symptom fatigue [3, 11, 32, 39, 35] [6, 1, 24, 5, 38] [7, 2, 34, 45, 40] [26, 12, 44, 9, 10, 33] [30, 28, 8]. The later references are selected as the studies for the meta-analyse conducted in this paper concerning fatigue prevalence. Some other characteristics are extracted from these studies: patients mean age, % of female, sample size, year of study, state of the study and how long the patient is followed since first diagnostic confirmed "Covid-19". Given the paper size consideration, we do not provide all the details of the data and the selection procedure. In summary, studies are published in English between years of 2020 and 2022 on Web of Science, Google/Google scholar, which containing specific terms like: "Post Covid Fatigue", "Long Covid Fatigue" or "Prevalence Fatigue" with publishers. Among the 1764 retrieved papers, we selected those dealing with prevalence of symptoms that contains fatigue of individuals that have confirmed "Covid-19" after at least four weeks since the first diagnostic. After screening and analyzing titles, abstract or full text of those articles, 25 articles were be included to our systematic review and meta-analysis. Sample sizes ranged from 39 to 1950. The mean of age samples is between 11 and 73.18, and median or mean follow up periods ranged from 4 weeks and 12 weeks.

4.1 Classical Meta-Analyse for Fatigue Prevalence

We performed a meta-analysis of fatigue prevalence using the *packages* "meta" and "metafor" from R software. The results are presented in Figure 1 by region then for all the studies. Regarding the variable introduced to measure effect size, i.e. transformed prevalence (see Equation (2)), the further the estimated value for the transformed prevalence is to the right of zero, the more prevalent the symptom of fatigue is. As an example, the first line of the region "USA" in

Figure 1 represents the result of the study proposed by the authors of logue *et. al.*. On the right, we can read the transformed prevalence estimate as well as

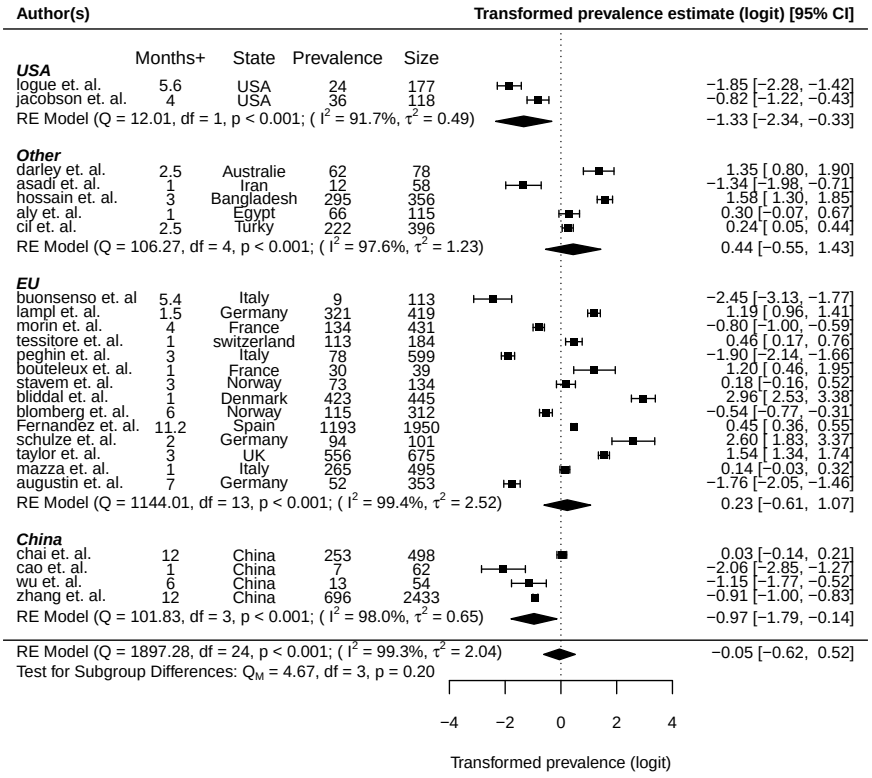

Fig. 1. Meta-analysis for all studies and individual groups by region

its confidence interval (see Equation (4). In this single study, it is clearly appears that fatigue is not a prevalent symptom of long-term covid. The last line in the result representing a region shows the results of the random effect model concerning this region while at the bottom of the figure, the results of the random effect regarding all the studies is represented. The Figure 1 shows a large disparity between the estimated values across all studies. Indeed, the result of combining studies based on the random effect model gives an overall estimate of -0.20 for the transformed prevalence with 95% confidence interval $[-0.87, 0.46]$. This "weighted average" overall estimate is very far from the results of most of the considered studies and the 95% confidence interval of the overall prevalence estimate does not intersect with several 95% confidence intervals of the individual estimates. The poor overlap of the confidence intervals signifies the presence

of statistical heterogeneity. This is confirmed by the the Cochran's Q test for heterogeneity as the p-values in Figure 1 are very low. Also the quantification of inconsistency across studies to assess the impact of heterogeneity shows, using I^2 indicator, the existence of considerable heterogeneity within all studies as well as within groups of studies, i.e. $I^2 > 99\%$. Finally, from the results shown in Figure 1, two groups tend to do not confirm the fatigue symptom prevalence (China and USA) while two others confirm the prevalence. Further clusters were tested regarding the number of months after a confirmed "Covid-19" (see column Months+ in Figure 1) but, as one can see in Table 1, the results about heterogeneity remain the same. For these clusters, months from 1 to 3 confirm prevalence of fatigue symptom. Note that with this approach we cannot confirm these results given the considerable heterogeneity in the identified groups. As they are based only on the aggregated mean estimates that indicate whether or not the prevalence of fatigue is confirmed. In addition, we used the Multivariate

Table 1. Results of two level Random effect model considering "months+" clusters

Months	# studies	T.P estimate [95% CI]	Test for Heterogeneity	I^2
1 to 3	15	$0.565[-0.171, 1.3]$	Q(df = 14) = 858.2, p-val < .001	98.88%
4 to 6	6	$-1.227[-1.794, -0.661]$	Q(df = 5) = 49.871, p-val < .001	93.62%
more than 6	4	$-0.54[-1.506, 0.425]$	Q(df = 3) = 558.892, p-val < .001	99.56%

Meta-Analysis Model of "metafor" package to perform three levels meta-analyses considering the factors region and number of months. It results on small variance 0.19 within-level of region factor versus 1.933 for all of studies but large variance 0.732 between levels compared to those of "months+" factor.

4.2 The Results of the Possibilistic Meta-Analysis Approach

The approach based on possibility distributions attempts to keep all of the information provided by each source throughout the meta-analysis process, in the representation then in the combination. Unlike the classical approach, there is no a priori hypothesis on the clusters or coherent sources but we use the MCS technique to determine the subset of coherent sources from the data. The information extracted from the data for each source consists of three confidence intervals A_1^k (0.05), A_2^k (0.5), A_3^k (0.95), A_4^k (1). Note that, in absence of information about the reliability of the sources, ω_k is fixed at 1 for all studies. Figure 2 represents the combination of Equation (6) for all the maximum coherent groups. As one can see, three kinds of groups can be distinguished: group 1 and 2 that do not confirm the prevalence of fatigue; group from 3 to 7 that have divided opinion; while group 8, 9 and 10 confirm prevalence of fatigue. Five maximum coherent groups are represented in Table 2 as they represent two trends in the data as one can see in Figure 2. Note that, some studies are part from several groups as they are linked to every overlapping studies. It is interesting to see in

Table 2. Some Maximum coherent subsets

Group	authors	Region	months+	authors	Region	months+
Group 1	buonsenso et. al.	EU	5.4	augustin et. al.	EU	7
	cao et. al.	China	1.0	peghin et. al.	EU	3
	asadi et. al.	Other	1.0	jacobson et. al.	USA	4
	logue et. al.	USA	5.6	morin et. al.	EU	4
	wu et. al.	China	6.0			
Group 2	buonsenso et. al.	EU	5.4	augustin et. al.	EU	7
	cao et. al.	China	1.0	jacobson et. al.	USA	4
	asadi et. al.	Other	1.0	morin et. al.	EU	4
	logue et. al.	USA	5.6	zhang et. al.	China	12
	wu et. al.	China	6.0	blomberg et. al.	EU	6
Group 8	bouteleux et. al.	EU	1	darley et. al.	Other	2.5
	stavem et. al.	EU	3	Fernandez et. al.	EU	11.2
	aly et. al.	Other	1	lampl et. al.	EU	1.5
	tessitore et. al.	EU	1	schulze et. al.	EU	2
	cil et. al.	Other	2.5			
Group 9	bouteleux et. al.	EU	1	lampl et. al.	EU	1.5
	stavem et. al.	EU	3	schulze et. al.	EU	2
	aly et. al.	Other	1	hossain et. al.	Other	3
	tessitore et. al.	EU	1	taylor et. al.	EU	3
	darley et. al.	Other	2.5			
Group 10	bouteleux et. al.	EU	1	bliddal et. al.	EU	1
	darley et. al.	Other	2.5	schulze et. al.	EU	2
	hossain et. al.	Other	3	taylor et. al.	EU	3

Table 2 that groups 1 and 2 have some close characteristics as they contain all the studies concerning the regions 'USA' and 'China'. In addition, these groups have majority of studies with the characteristics 'months+' that is higher than four months. While group 8, 9 and 10 contain exclusively studies from 'EU' and 'Other' and the characteristics 'months+' is less than 3 months except for one study. Finally these results suggest that when the clinical status of the patients is followed more than four months the fatigue symptom is not persisting ? Note that the advantage of the possibilistic approach is that the homogeneous groups were identified from the data via the maximal coherent subsets approach. the confirmation or not of the prevalence for certain regions is determined by their membership of coherent groups. For example, China and USA belong to groups 1 and 2 that are both do not confirm fatigue prevalence. The non-confirmation is more stronger with group 1 than group 2.

5 Conclusion

We carried out two meta-analyses on data concerning the prevalence of fatigue in patients suffering from "post-covid" syndromes. The first based on the classical statistical approach and the second based on the possibilistic approach. In both meta-analyses, we identified trends depending on the region of the analysis or

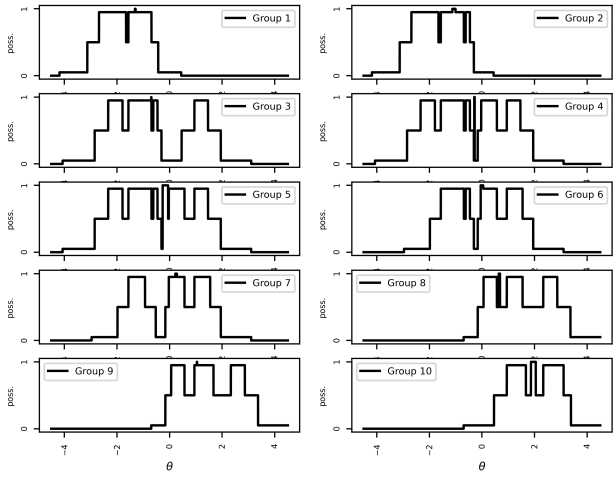

Fig. 2. Merging coherent sources information

the number of months of patient follow-up. The USA and China regions do not confirm the prevalence of fatigue while the Europe and other countries regions confirm it. Also, with regard to patient follow-up, studies in which patients were followed for more than four months do not confirm the prevalence of Fatigue. With the statistical approach we cannot confirm these results given the considerable heterogeneity in the identified groups. Whereas in the possibilistic approach the homogeneous groups were identified from the data via the maximal coherent sets approach. confirmation or disconfirmation of prevalence for certain regions is determined by their membership in coherent groups. For example, China and the USA belong to groups 1 and 2 (see Table 2)

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