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Original Article

A tool to measure complexity in public health interventions: Its statistical properties and meta-regression approach to adjust it in meta-analysis

N. Ravishankar^a, N. Sreekumaran Nair^{b,*}^a PhD Scholar, Department of Statistics, Level 6, Health Science Library Building, Manipal University, Manipal 576104, India^b Director, Public Health Evidence South Asia (PHESA), Professor of Biostatistics and Head, Department of Statistics, Level 6, Health Science Library Building, Manipal University, Manipal 576104, Karnataka State, India

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ABSTRACT

Background: Public health interventions are conventionally cited as a popular example of complex interventions. Complexity of public health interventions has always been an obstacle for the meta-analysis of these studies. Earlier an attempt was made by Public Health Evidence South Asia (PHESA) to numerically measure the complexity in public health interventions by a tool. This study is an extension of that initiative which aims to investigate various statistical distributional properties of the complexity score and adjust the measured complexity in meta-analysis.

Methods: Complexity score of 71 studies was used to identify the best probability distribution that fits the complexity score, study its sampling distribution and determine the optimum power transformation. Meta-regression was employed to adjust the measured complexity in meta-analysis.

Results: Lognormal distribution was observed to be an ideal probability distribution for the complexity score, the sampling distribution of the mean of complexity score was found to be normally distributed and the optimum power transformation for the complexity score was '−0.42'. The raw estimate from random effects meta-analysis was found to be −0.05, 95% CI −0.14 to 0.04, whereas the estimate adjusted for complexity from meta-regression was −0.048, 95% CI −0.13 to 0.03. There was a reduction in the proportion of heterogeneity (I^2 – squared) after adjusting for complexity (73.01%–66.30%), indicating that complexity had an impact on the effect estimates of studies.

Conclusion: The concept of measuring the inherent complexity and adjusting it in meta-analysis adds novelty to the existing meta-analysis approach. This innovative approach is likely to create a new dimension for meta-analysis of complex community level

* Corresponding author at: Public Health Evidence South Asia (PHESA), Department of Statistics, Level 6, Health Science Library Building, Manipal University, Manipal 576104, Karnataka State, India. Tel.: +91 9900133734.

E-mail addresses: ravi8133@gmail.com (N. Ravishankar), sree.nair@manipal.edu (N. Sreekumaran Nair).

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interventions and provide more precise evidence. However, further methodological research and piloting is required to establish the validity and sensitivity of this approach.

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1. Introduction

Complexity is the characteristic of a phenomenon of being present in a complicated network of numerous components, where there is an opportunity for the components to interact with each other. As a consequence, it would be idealistic to define the most active component and figure out which component or combinations of components is pivotal in achieving the outcome/s. Public health interventions are conventionally cited as a popular example of complex interventions. They are intended to upkeep the health of the community and are delivered at the level of population. The innate characteristics of these interventions to cater to an outstretched population, encompass a bundle of activities and contextual confinement entrusts complexity.¹ Important sources responsible for complexity in public health interventions are (1) The number of interacting components within the experimental and control interventions (2) The number and difficulty of behaviours required by those delivering or receiving the intervention (3) Number of groups or organizational levels targeted by the intervention (4) Number and variability of outcomes (5) Degree of flexibility permitted in the tailoring of the intervention. Other than these factors, the presence of non-linear causal pathways between intervention and outcome (i.e., change in outcome not proportional to change in intervention) is an additional and a key source of complexity.^{2–4}

Systematic reviews involve a prudently selected focused research question and yield comprehensive evidence by capturing all available relevant published studies on the concerned research question.⁵ Systematic review methodology involves scientific processes to collect, combine, analyze and summarize all available evidence with minimum or no bias. Meta-analysis is a statistical technique by which the quantitative results from several studies are integrated to yield a summary result.⁶ Systematic review combined with meta-analysis has been accepted as a potential robust method of health care research evidence synthesis.⁵

Complexity of public health interventions has always been an obstacle for the meta-analysis of these studies.¹ Further, it is more likely to mask the true effect in meta-analysis of public health interventions. Therefore measuring this complexity and adjusting the measured complexity in meta-analysis using a suitable statistical technique is a required strategy to counter this limitation. Earlier an attempt was made by the Public Health Evidence South Asia (PHESA) to numerically measure the complexity in public health interventions by means of a tool.¹ The tool was developed focussing four primary domains of complexity namely population, intervention, context and outcome. The items included in the tool were segregated after a meticulous examination of published public health interventions. The scoring pattern was set for

each item based on its importance and number of options such that, higher score reflects a higher complexity. The scores of all items of a domain were added to obtain domain specific complexity score and addition of complexity scores of all four domains presented the total complexity score for the study.

As an extension of the complexity tool development endeavour, this study is meant to investigate the statistical distributional properties of the complexity score and adjust the measured complexity in meta-analysis using meta-regression.

2. Methodology

Eight diverse Cochrane public health systematic reviews were identified^{7–14} as a pathway to obtain the studies pertaining to public health interventions. From these systematic reviews 71 such studies were retrieved. The selected studies were subjected to complexity assessment using the PHESA tool and the corresponding total complexity scores were obtained, which formed the basis of this work. The average complexity score of 71 studies was 35.23, with a minimum score of 20 and a maximum of 83.

The methodology has been substantiated under two broad sub-sections.

2.1. Statistical distributional properties

2.1.1. Distribution fitting – identifying the ideal or best probability distribution that fits the total complexity score

A histogram was constructed to identify the distributions that are likely to fit the total complexity score. Based on the shape of the histogram, a list of such distributions was generated. Later, the parameters of the anticipated distributions were estimated by maximum likelihood technique. Anderson-Darling (AD) goodness of fit test was used to evaluate the quality of fit i.e., to decide which among the anticipated distributions is the best fit. Higher P-value (>0.05) or a lower test statistic value was the criterion adopted to decide the best fit.^{15,16}

2.1.2. Studying the sampling distribution of the mean of total complexity score

Bootstrapping method was employed to explore the sampling distribution of the mean of total complexity score. One thousand boot strap samples of the same size were generated from the complexity scores. These samples were selected by simple random sampling with replacement.¹⁷

2.1.3. Box-Cox transformation

Box-Cox transformation¹⁸ was used to normalize the total complexity score. It is given by;

$$y_i^{(\lambda)} = \begin{cases} \frac{y_i^\lambda - 1}{\lambda} & \text{if } \lambda \neq 0 \\ \ln(y_i) & \text{if } \lambda = 0 \end{cases} \quad i = 1, 2, \dots, n(\text{no. of observations}) \quad (1)$$

y is the variable to be subjected to transformation.

The optimum power transformation is decided based on the λ value.

2.2. Adjusting the measured complexity in meta-analysis: the meta-regression

Meta-regression is the statistical method to explore the impact of covariates on effect estimates of studies included in meta-analysis. It involves a weighted linear regression between the dependent variable, which is the effect estimate of studies and one or more study level covariates and weights $W_i = 1/V_i$ where, W_i is the weight assigned to i^{th} study and V_i is the variance of effect estimate of i^{th} study.¹⁹

Meta-regression was carried out for 14 studies of the Cochrane public health systematic review “Interventions for preventing obesity in children¹⁴” included under meta-analysis for the outcome “change in body mass index”. Initially a traditional random effects meta-analysis was performed and later meta-regression was performed for the same studies with standardized mean difference (SMD) as the dependent variable and total complexity score as the independent variable. Following meta-regression model was used;

$$Y_i = \beta_0 + \beta_1(X_i - \bar{X}) + U_i, \quad i = 1, 2, 3, \dots, k \text{ studies} \quad (2)$$

The independent variable is centered at its mean such that the estimate of intercept provides the pooled estimate after adjusting for complexity.

3. Results

The results are presented in accordance with the two sub sections of methodology.

3.1. Distribution fitting

The histogram of total complexity score of 71 studies has been presented in Fig. 1. Based on the shape of the histogram, Normal distribution, Gamma distribution, Lognormal distribution and Weibull distribution was considered as a possible fit for the total complexity score. Estimates of the parameters of the anticipated distributions are presented in Table 1. Value of the AD test statistic with corresponding P-values for all anticipated distributions is depicted in Table 2. Out of the four anticipated distributions, the lognormal distribution was considered as the best fit as it possessed the lowest AD test statistic value/highest P-value than other distributions (Fig. 2).

3.2. Sampling distribution of the mean of total complexity score

One thousand bootstrap samples were drawn to determine the sampling distribution of the mean of total complexity score. It

Fig. 1 – Histogram of complexity score of 71 studies. The distributions that could possibly fit the complexity score were anticipated by considering the shape of the histogram.

was observed to be normally distributed with a mean of 35.31, standard deviation 1.22 and 95% confidence interval (CI) 32.97 to 37.67. Fig. 3 presents the histogram of the sampling distribution of the mean of total complexity score.

3.3. Box-Cox transformation

Several λ values were computed from -2 to 2 at an interval of 0.01 . The optimum λ value was found to be -0.42 . The skewness of total complexity score before and after transformation was 1.43 and -0.02 respectively. The histogram of transformed total complexity score is shown in Fig. 4.

3.4. Meta-regression

Random effects meta-analysis of 14 studies for the outcome “change in body mass index” of the Cochrane systematic review “Interventions to prevent obesity in children¹⁴” yielded a pooled estimate of -0.05 with 95% CI -0.14 to 0.04 . The Chi-squared statistic for heterogeneity was found to be significant ($P = 0.001$), I^2 = 73.01% and the estimate of between-study variance Tau-squared was equal to 0.0154 . The meta-regression model was also fitted for the same set of studies by centering the complexity score at its mean. Table 3 consists of results of meta-regression.

Table 1 – Parameters estimated by maximum likelihood estimation method.

Distribution	Parameters	
Normal distribution	Mean:35.32	SD:10.33
Gamma distribution	Shape:13.23	Scale: 0.37
Lognormal distribution	Mean-log: 3.52	SD-log: 0.27
Weibull distribution	Shape: 3.32	Scale: 39.09

Table 2 – AD test statistic values with corresponding P-values for the anticipated distributions.

Distribution	Anderson-darling test statistic value	P-value
Normal	0.985	0.013
Gamma	0.409	0.250
Lognormal	0.313	0.541
Weibull	1.537	0.01

Bold indicates that the distribution is the best fit.

The pooled estimate adjusted for complexity was found to be “−0.048 with 95% CI −0.13 to 0.03”. I – squared statistic in this case was 66.30% and Tau – squared was 0.0102. Forest plot showing the unadjusted pooled estimate and the pooled estimate adjusted for complexity is depicted in Fig. 5.

4. Discussion

The word complexity and public health interventions go hand-in-hand. They are multi-faceted interventions which seek a grass root delivery to a vast heterogeneous population and comprise a bundle of activities, where it may not be possible to separately study the influence of individual components. The complexity is an important factor which renders the results of a public health intervention not generalizable.²⁰ Systematic reviews and meta-analysis mark the current vogue in health care evidence synthesis. The evidence generated by them is considered to be superior to that of any other study design.⁵ Systematic reviews and meta-analysis cater to the evidence needs of all major health care decisions including health care policies and programmes. The complexity is more likely to mask the true effect in meta-analysis of public health interventions and thus behaves as a barrier for the meta-analysis of such interventions.¹ Several international organizations like Cochrane collaboration (www.cochrane.org), Medical Research Council (MRC), UK, (www.mrc-bsu.cam.ac

Fig. 3 – Sampling distribution of the mean of complexity score. Histogram of sampling distribution of the mean of complexity score.

uk) and others have been engaged in extensive research activities to develop appropriate methods to handle this complexity.

The Public Health Evidence South Asia (PHESA), the South Asian Satellite of Cochrane Public Health Group (CPHG) has been instrumental in proposing an alternate approach of meta-analysis for complex public health interventions, which includes measuring or quantifying the complexity and later adjusting the measured complexity in meta-analysis. PHESA has developed a tool to measure the complexity in public health interventions.¹ The tool intends to capture the complexity of all four major domains namely population, intervention, context, outcome and the scoring pattern is set in direct proportion with the complexity. The present paper aims to investigate the statistical distributional properties of

Fig. 2 – Distribution fitting. Probability density curves of all the four anticipated distributions (Normal distribution, Gamma distribution, Lognormal distribution, Weibull distribution) that could fit the complexity score.

Fig. 4 – Box–Cox transformation. Histogram of transformed complexity score.

Table 3 – Results of meta-regression.

Regression coefficient	Value	95% CI
Intercept	−0.048	(−0.128, 0.031)
Slope	−0.004	(−0.021, 0.013)

the complexity score i.e., identifying the ideal distribution for the complexity score, study of its sampling distribution, Box–Cox transformation and further adjusting the measured complexity in meta-analysis using meta-regression technique.

The complexity scores from 71 publications contributed by eight diverse Cochrane public health systematic reviews were utilized for the present study. The lognormal distribution was deemed to be the best fit for the total complexity score. According to “Medical Research Council (MRC), UK guidance²⁰”, the presence of non-linear causal pathways between intervention and outcome (i.e., change in outcome not proportional to change in intervention) is one of the important sources leading to complexity. In other words, complexity is created when a large number of factors act in a multiplicative way. Theoretically, lognormal distribution is a good candidate if several factors influence the value of a variable in a multiplicative manner.²¹ The sampling distribution of the mean of complexity score was found to be normally distributed and the optimum power transformation was $\lambda = -0.42$.

Meta-regression technique was employed to adjust the measured complexity in meta-analysis. Borenstein et al quote that “meta-regression follows the same approach as simple/multiple linear regression except that the dependent and independent variables are measured at the unit of study rather than at the level of subject”.¹⁹ It is one of the effective approaches to determine the relationship between study level covariates and the effect estimates of studies included under meta-analysis. In the present study, the pooled estimate adjusted for complexity was obtained as the estimate of intercept after centering the complexity score at its mean (subtracting the mean complexity score of all studies from the complexity score of each study included under meta-analysis). The model was fitted to 14 studies of a Cochrane Public Health Systematic review “Interventions to prevent obesity in children¹⁴” for the outcome “change in body mass index”. The estimate adjusted for complexity was found to be −0.048, 95% CI −0.13 to 0.03, while the raw estimate from random effects meta-analysis was −0.05, 95% CI −0.14 to 0.04.

Fig. 5 – Forest Plot. Close comparison of unadjusted pooled estimate and the pooled estimate adjusted for complexity.

However, it is interesting to note that there was a reduction in the proportion of heterogeneity (I^2 -squared) after adjusting for complexity (73.01%–66.30%), indicating that complexity had an impact on the effect estimates of studies.

5. Limitation of the study

It is evident from the meta-regression analysis that the adjusted estimate differs from the raw estimate only by a small amount. The major limitation of the study is that the meta-regression was applied to adjust for complexity in only one situation. It requires further piloting to understand the sensitivity of the approach. However this limitation will be addressed in our future publications.

6. Conclusion

The concept of measuring the inherent complexity and adjusting it in meta-analysis adds novelty to the existing meta-analysis approach. This innovative approach is likely to create a new dimension for Meta-analysis of complex community level interventions and provide more precise evidence. However, further methodological research and piloting is required to establish the validity and sensitivity of this approach.

Contributions

Ravishankar N – responsible for exploration of the statistical distributional properties, meta-regression and preparation of the manuscript.

Dr. N. Sreekumaran Nair – Mentor, conceived the problem, evaluated at each stage of the project, edited the manuscript and provided general expert guidance.

Conflicts of interest

All authors have none to declare.

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