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The Random-Effect Model of Bivariate Meta-Analysis Based on the Difference Mean

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Abstract

In this paper, we establish the random-effect model of bivariate meta-analysis based on the difference mean. Under the assumption of the multilevel normal distribution of the difference mean, we obtain the maximum likelihood estimator $\hat{\mu}_{ML}$ of the difference mean by the method of maximum likelihood estimate. We conclude that the maximum likelihood estimator $\hat{\mu}_{ML}$ of the difference mean is unbiased for the difference mean effect μ. In addition, we get the corresponding covariance matrix and the $(1-\alpha)100\%$ confidence interval for the difference mean effect μ.

Keywords

Meta-Analysis, Maximum Likelihood Estimate, Random-Effect Model

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基于均差估计二变量Meta-分析的随机效应模型

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摘　要

本文给出已知协方差矩阵的基于均差估值的二变量Meta-分析随机效应模型，并通过极大似然估计法给出效应量估计并说明了其无偏性。通过计算估计效应量的协方差矩阵，给出估计效应分量的$(1-\alpha)100\%$置信区间。

关键词

Meta-分析，极大似然估计，随机效应模型

1. 前言

Meta-分析是一种对同一问题的不同研究进行定量合并的一种方法。该方法是通过考虑每个研究内和研究间的差异性以及研究发表偏倚性得到一个综述结果，从而解决了单个研究样本量小，区域、种族差异大等的缺点。因此 Meta-分析的结果对很多领域的科学研究都具有指导意义。针对具体问题的 Meta-分析及其统计方法研究已持续了一个世纪之久。最早是在 1904 年 Karl Pearson 针对伤寒疫苗效果进行了合并研究[1]；接下来的很多年中对某些零星的问题做了类似的综合[2]。但是在过去的四十年中，人们逐渐意识到医学实验和临床操作需要基于整体的相关性和可靠证据，Meta-分析的影响得到极大的扩展[3]。仅在 2018 年，关于健康管理的 Meta-分析发表文章将近 4000 篇。

虽然 Meta-分析在很多领域都有很好的应用，但对 Meta-分析本身的统计方法研究与其应用研究相比就少了很多。从广泛应用的意义上来讲，Meta-分析是以估计量的标准误差为权重的点估计加权平均。随机效应模型的 Meta-分析在各个研究效应量不相等这一假设，具体是以估计量方差及研究间差异方差和的

逆作为权重得到的加权平均效应量，并可扩展为合并研究间协变量估计[4]。

随着数据科学的快速发展，数据维度和数据量急速增加导致单变量 Meta-分析无法满足现实应用的需求。多变量 Meta-分析有许多优点：第一，可以在一个模型框架下得到所有效应量的估计量；第二，可以通过所有效应量的估计量的协方差矩阵描述多效应量之间的关系。第三，可以获得具有更好统计特性的参数估计量；第四，我们可以获得区别于单变量 Meta-分析的潜在机理原因；第五，多变量分析的方法可以在一定程度上降低纳入文献的偏倚性。

由于多变量 Meta-分析与单变量 Meta-分析比较起来有很多的优点，因此多变量 Meta-分析在各个领域的应用研究是很多的。然而，对于多变量 Meta-分析本身统计方法的研究却很少。1988 年，为了研究教练在 SAT 中的作用，Raudenbush SW 等人通过广义最小二乘法建立了多效应量合并的模型[5]；1993 年，van Houwelingen HC 等人在文献[6]首次给出了基于比值比的二变量 Meta-分析模型，并讨论了该模型的异质性检验和敏感性分析；1996 年，Kalaian HA 等人为了研究教练在 SAT 语言和数学方面的指导效果，在文献[7]建立了基于比值比的各研究内效应量不同情形下的多元 Meta-分析模型，并通过 REML 方法估计了效应量的协方差矩阵；2002 年，van Houw -elingen HC 等人在广义多元混合线性模型的框架下，通过似然估计方法给出了多元 Meta-回归模型，并将此模型扩展到了非正态分布情形[8]。2008 年，Riley RD 等人在文献[9]中通过极大似然估计法给出了一些特殊相关系数情形下的二变量 Meta-分析的协方差矩阵估计；2008 年，Ritz J 等人在文献[10]中通过极大似然估计和估计方程给出了协方差矩阵已知情形下的多元效应量回归参数，并将此模型应用到肺癌发病率的临床推断中。2010 年，Paul M 等人在文献[11]中通过基于可积嵌套拉普拉斯近似的贝叶斯方法给出了多元 Meta-分析的合并效应量估计，这种方法得到的方差估计偏移量更小且稳定。

本文通过极大似然估计法给出已知协方差矩阵的基于均差估值的二变量 Meta-分析随机效应模型，并通过极大似然估计法给出效应量估计。通过计算估计效应量的协方差矩阵，给出效应分量的 $(1-\alpha)100\%$ 置信区间。

2. 问题描述

在协方差矩阵的基于均差估值的二变量 Meta-分析随机效应模型中，我们假设个体量 X_{i1j}^{C}，X_{i1j}^{T}，X_{i2j}^{C} 和 X_{i2j}^{T} 是独立的并且是正态分布，其均值分别为 μ_1^{C}，μ_1^{T}，μ_2^{C} 和 μ_2^{T}，每个研究内的方差分别为 σ_{i1}^2，σ_{i2}^2。因此 $\bar{X}_{i1}^{C}$，$\bar{X}_{i1}^{T}$，$\bar{X}_{i2}^{C}$ 和 $\bar{X}_{i2}^{T}$ 是独立的且服从正态分布，其均值分别为 μ_1^{C}，μ_1^{T}，μ_2^{C} 和 μ_2^{T}，方差分别为 $\frac{\sigma_{i1}^2}{n_{i1}^{C}}$，$\frac{\sigma_{i1}^2}{n_{i1}^{T}}$，$\frac{\sigma_{i2}^2}{n_{i2}^{C}}$，$\frac{\sigma_{i2}^2}{n_{i2}^{T}}$。

由上述假设，均差效应量 $\boldsymbol{D}_i$ 的分布可表示为：

$$\boldsymbol{D}_i=\begin{pmatrix} D_{i1} \\ D_{i2} \end{pmatrix} \sim N\left(\begin{pmatrix} \mu_1 \\ \mu_2 \end{pmatrix},\begin{pmatrix} \sigma_{i1}^2 w_{i1}+\tau^2 & \rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma \\ \rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma & \sigma_{i2}^2 w_{i2}+\gamma^2 \end{pmatrix}\right)$$

其中 $\mu_1=\mu_1^{T}-\mu_1^{C}$，$\mu_2=\mu_2^{T}-\mu_2^{C}$ 为均值，$w_{i1}=\frac{1}{n_{i1}^{T}}+\frac{1}{n_{i1}^{C}}$，$w_{i2}=\frac{1}{n_{i2}^{T}}+\frac{1}{n_{i2}^{C}}$ 及 ρ_0 是非随机的。一般地，μ_1，μ_2 为未知参数。本文主要内容是通过极大似然估计法来估计 μ_1，μ_2。为了方便讨论，记 $\boldsymbol{S}_i=\begin{pmatrix} \sigma_{i1}^2 w_{i1} & \rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}} \\ \rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}} & \sigma_{i2}^2 w_{i2} \end{pmatrix}$ 为研究内均值效应量的协方差矩阵；$\Sigma=\begin{pmatrix} \tau^2 & \rho_1\tau\gamma \\ \rho_1\tau\gamma & \gamma^2 \end{pmatrix}$ 为描述研

究间关系的协方差矩阵。

3. 均值效应量的极大似然估计

根据之前的假设效应量 $\boldsymbol{D}_i$ 服从正态分布，因此关于 $\boldsymbol{\mu}$ 的似然函数为：

$$L\left(\boldsymbol{\mu},\boldsymbol{D}_i,\boldsymbol{S}_i\right)=\prod_{i=1}^{k}\frac{1}{2\pi det\left(\boldsymbol{S}_i+\Sigma\right)^{\frac{1}{2}}}\exp\left\{-\frac{\left(\boldsymbol{D}_i-\boldsymbol{\mu}\right)^{\mathrm{T}}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\left(\boldsymbol{D}_i-\boldsymbol{\mu}\right)}{2}\right\}$$

其中 $\boldsymbol{\mu}=\begin{pmatrix}\mu_1\\ \mu_2\end{pmatrix}$， $\boldsymbol{S}_i+\Sigma=\begin{pmatrix}\sigma_{i1}^2w_{i1}+\tau^2 & \rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma\\ \rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma & \sigma_{i2}^2w_{i2}+\gamma^2\end{pmatrix}$。其所对应的对数似然函数为：

$$\ln L\left(\boldsymbol{\mu},\boldsymbol{D}_i,\boldsymbol{S}_i\right)=-k\ln\left(2\pi\right)-\frac{1}{2}\sum_{i=1}^{k}\ln\left[det\left(\boldsymbol{S}_i+\Sigma\right)\right]-\frac{1}{2}\sum_{i=1}^{k}\left(\boldsymbol{D}_i-\boldsymbol{\mu}\right)^{\mathrm{T}}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\left(\boldsymbol{D}_i-\boldsymbol{\mu}\right)$$

定理 3.1：设效应量 $\boldsymbol{D}_i$ 服从 $N\left(\begin{pmatrix}\mu_1\\ \mu_2\end{pmatrix},\begin{pmatrix}\sigma_{i1}^2w_{i1}+\tau^2 & \rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma\\ \rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma & \sigma_{i2}^2w_{i2}+\gamma^2\end{pmatrix}\right)$ 的正态分布，则 $\boldsymbol{\mu}$ 的极大似然估计量的分量为：

$$\begin{aligned}\hat{\mu}_1=&\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)\right.\right.\\&\left.-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right.\\&\left.\left.\times\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\right\}^{-1}\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\right.\\&\times\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left\{\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)\right.\right.\\&\left.-\left(\rho_1\tau\gamma+\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right]D_{j1}\\&\left.\left.-\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\right]D_{j2}\right\}\right\}\end{aligned}$$

$$\begin{aligned}\hat{\mu}_2=&\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\right.\right.\\&\left.-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right.\\&\left.\left.\times\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\right\}^{-1}\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\right.\\&\times\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left\{\left[\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right.\right.\\&\left.\times\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right]D_{j1}\\&\left.\left.-\left[\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)-\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\right]D_{J2}\right\}\right\}\end{aligned}$$

证明：因为关于 $\boldsymbol{\mu}$ 的似然函数为：

$$L\left(\boldsymbol{\mu},\boldsymbol{D}_i,\boldsymbol{S}_i\right)=\prod_{i=1}^{k}\frac{1}{2\pi det\left(\boldsymbol{S}_i+\Sigma\right)^{\frac{1}{2}}}\exp\left\{-\frac{\left(\boldsymbol{D}_i-\boldsymbol{\mu}\right)^{\mathrm{T}}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\left(\boldsymbol{D}_i-\boldsymbol{\mu}\right)}{2}\right\}$$

其所对应的对数似然函数为：

$$\begin{aligned}\ln L\left(\boldsymbol{\mu},\boldsymbol{D}_i,\boldsymbol{S}_i\right)&=-k\ln\left(2\pi\right)-\frac{1}{2}\sum_{i=1}^{k}\ln\left[det\left(\boldsymbol{S}_i+\Sigma\right)\right]-\frac{1}{2}\sum_{i=1}^{k}\left(\boldsymbol{D}_i-\boldsymbol{\mu}\right)^{\mathrm{T}}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\left(\boldsymbol{D}_i-\boldsymbol{\mu}\right)\\
&=-\frac{1}{2}\sum_{i=1}^{k}\ln\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]\\
&\quad-\frac{1}{2}\sum_{i=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\\
&\quad\times\left[\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\left(D_{i1}-\mu_1\right)^2-2\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right.\\
&\quad\left.\times\left(D_{i1}-\mu_1\right)\left(D_{i2}-\mu_2\right)+\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(D_{i2}-\mu_2\right)^2\right]-k\ln\left(2\pi\right)\end{aligned}$$

上述对数似然函数对 μ_1， μ_2 的偏导数为：

$$\begin{aligned}\frac{\partial\ln L\left(\boldsymbol{\mu},\boldsymbol{D}_i,\boldsymbol{S}_i\right)}{\partial\mu_1}&=\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\\
&\quad\times\left[\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\left(D_{i1}-\mu_1\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\left(D_{i2}-\mu_2\right)\right]\end{aligned}$$

$$\begin{aligned}\frac{\partial\ln L\left(\boldsymbol{\mu},\boldsymbol{D}_i,\boldsymbol{S}_i\right)}{\partial\mu_2}&=\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\\
&\quad\times\left[-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\left(D_{i1}-\mu_1\right)+\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(D_{i2}-\mu_2\right)\right]\end{aligned}$$

令 $\dfrac{\partial\ln L\left(\boldsymbol{\mu},\boldsymbol{D}_i,\boldsymbol{S}_i\right)}{\partial\mu_1}=0,\dfrac{\partial\ln L\left(\boldsymbol{\mu},\boldsymbol{D}_i,\boldsymbol{S}_i\right)}{\partial\mu_2}=0$ 即得：

$$\begin{aligned}&\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\\
&\times\left[\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\left(D_{i1}-\mu_1\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\left(D_{i2}-\mu_2\right)\right]=0\end{aligned}$$

$$\begin{aligned}&\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\\
&\times\left[-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\left(D_{i1}-\mu_1\right)+\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(D_{i2}-\mu_2\right)\right]=0\end{aligned}$$

整理可得：

$$\begin{aligned}&\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left(\sigma_{i2}^2+\gamma^2\right)\omega_{i2}\mu_1\\
&-\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\mu_2\\
&=\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left(\sigma_{i2}^2+\gamma^2\right)\omega_{i2}D_{i1}\\
&\quad-\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)D_{i2}\end{aligned}$$

因为 $\boldsymbol{S}_i+\Sigma=\begin{pmatrix}\sigma_{i1}^2 w_{i1}+\tau^2 & \rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma \\ \rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma & \sigma_{i2}^2 w_{i2}+\gamma^2\end{pmatrix}$ 可逆，且 $(\boldsymbol{S}_i+\Sigma)^{-1}$ 为：

$$\left[det(\boldsymbol{S}_i+\Sigma)\right]^{-1}\begin{pmatrix}\sigma_{i2}^2 w_{i2}+\gamma^2 & -\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma\right) \\ -\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma\right) & \sigma_{i1}^2 w_{i1}+\tau^2\end{pmatrix}$$

其中 $det(\boldsymbol{S}_i+\Sigma)=\left[\left(\sigma_{i1}^2 w_{i1}+\tau^2\right)\left(\sigma_{i2}^2 w_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}$，

因此上述关于 μ_1， μ_2 的线性方程组的解为：

$$\begin{aligned}\hat{\mu}_1=&\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\right.\right.\\&-\left.\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right.\\&\left.\left.\times\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\right\}^{-1}\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\right.\\&\times\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left\{\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)\right.\right.\\&-\left.\left(\rho_1\tau\gamma+\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right]D_{j1}\\&\left.\left.-\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\right]D_{j2}\right\}\right\}\end{aligned}$$

$$\begin{aligned}\hat{\mu}_2=&\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\right.\right.\\&-\left.\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right.\\&\left.\left.\times\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\right\}^{-1}\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\right.\\&\times\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left\{\left[\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right.\right.\\&\times\left.\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right]D_{j1}\\&\left.\left.-\left[\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)-\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\right]D_{J2}\right\}\right\}\end{aligned}$$

注：由 $(\boldsymbol{S}_i+\Sigma)^{-1}$ 为： $\left[det(\boldsymbol{S}_i+\Sigma)\right]^{-1}\begin{pmatrix}\sigma_{i2}^2 w_{i2}+\gamma^2 & -\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma\right) \\ -\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma\right) & \sigma_{i1}^2 w_{i1}+\tau^2\end{pmatrix}$，

其中 $det(\boldsymbol{S}_i+\Sigma)=\left[\left(\sigma_{i1}^2 w_{i1}+\tau^2\right)\left(\sigma_{i2}^2 w_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}$，

可以给出效应量 $\boldsymbol{D}_i$ 服从正态分布的合并效应量的矩阵形式为：

$$\hat{\boldsymbol{\mu}}_{ML}=\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{-1}\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\boldsymbol{D}_i\text{。}$$

由上述效应量 $\boldsymbol{D}_i$ 服从正态分布的合并效应量均值估计量分量的具体形式，我们可以得到合并效应量均值估计量的如下性质：

性质 2.1：设效应量设效应量 $\boldsymbol{D}_i$ 服从 $N\left(\begin{pmatrix}\mu_1\\ \mu_2\end{pmatrix},\begin{pmatrix}\sigma_{i1}^2 w_{i1}+\tau^2 & \rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma\\ \rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma & \sigma_{i2}^2 w_{i2}+\gamma^2\end{pmatrix}\right)$ 的正态分布，其极大似然估计量为：$\hat{\boldsymbol{\mu}}_{ML}=\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{-1}\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\boldsymbol{D}_i$，则 $\hat{\boldsymbol{\mu}}_{ML}$ 对于 $\boldsymbol{\mu}$ 是无偏的。

证明：要证明估计量的无偏性，需证等式 $E\left(\hat{\boldsymbol{\mu}}_{ML}\right)=\boldsymbol{\mu}$ 成立。根据我们给出的效应量 $\boldsymbol{D}_i$ 服从正态分布的合并效应量均值估计量分量的具体形式，我们需要证明 $E\left(\hat{\mu}_1\right)=\mu_1$，$E\left(\hat{\mu}_2\right)=\mu_2$。因为 $E\left(D_{i1}\right)=\mu_1$，$E\left(D_{i1}\right)=\mu_2$，所以

$$\begin{aligned}
E\left(\hat{\mu}_1\right)=E&\left\{\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\right.\right.\right.\\
&-\left.\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right.\\
&\times\left.\left.\left.\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\right\}^{-1}\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\right.\\
&\times\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left\{\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)\right.\right.\\
&-\left.\left(\rho_1\tau\gamma+\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right]D_{j1}\\
&-\left.\left.\left.\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\left(\sigma_{j1}^2\omega_{i1}+\tau^2\right)\right]D_{j2}\right\}\right\}\right\}
\end{aligned}$$

$$\begin{aligned}
=&\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\right.\right.\\
&-\left.\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right.\\
&\times\left.\left.\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\right\}^{-1}\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\right.\\
&\times\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left\{\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)\right.\right.\\
&-\left.\left(\rho_1\tau\gamma+\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right]E\left(D_{j1}\right)\\
&-\left.\left.\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\left(\sigma_{j1}^2\omega_{i1}+\tau^2\right)\right]E\left(D_{j2}\right)\right\}\right\}
\end{aligned}$$

$$
\begin{aligned}
=&\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)\right.\right.\\
&-\left.\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right.\\
&\times\left.\left.\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\right\}^{-1}\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\right.\\
&\times\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left\{\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)\right.\right.\\
&-\left.\left(\rho_1\tau\gamma+\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right]\mu_1\\
&-\left.\left.\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\left(\sigma_{j1}^2\omega_{i1}+\tau^2\right)\right]\mu_2\right\}\right\}
\end{aligned}
$$

$$
\begin{aligned}
=&\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)\right.\right.\\
&-\left.\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right.\\
&\times\left.\left.\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\right\}^{-1}\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\right.\\
&\times\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left\{\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)\right.\right.\\
&-\left.\left(\rho_1\tau\gamma+\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right]\mu_1\\
&-\left.\left.\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\right]\mu_2\right\}\right\}
\end{aligned}
$$

$$
\begin{aligned}
=&\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)\right.\right.\\
&-\left.\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right.\\
&\times\left.\left.\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\right\}^{-1}\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\right.\\
&\times\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)\right.\\
&-\left.\left.\left(\rho_1\tau\gamma+\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right]\right\}\mu_1\\
=&\,\mu_1
\end{aligned}
$$

$$E\left(\hat{\mu}_2\right)=E\left\{\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\right.\right.\right.$$

$$\left.-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right.$$

$$\left.\left.\times\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\right\}^{-1}\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\right.$$

$$\times\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left\{\left[\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right.\right.$$

$$\left.\times\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right]D_{j1}$$

$$\left.\left.\left.-\left[\left(\rho_1\tau\gamma+\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)-\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\right]D_{J2}\right\}\right\}\right\}$$

$$=\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\right.\right.$$

$$\left.-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right.$$

$$\left.\left.\times\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\right\}^{-1}\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\right.$$

$$\times\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left\{\left[\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right.\right.$$

$$\left.\times\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right]E\left(D_{j1}\right)$$

$$\left.\left.-\left[\left(\rho_1\tau\gamma+\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)-\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\right]E\left(D_{J2}\right)\right\}\right\}$$

$$=\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\right.\right.$$

$$\left.-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right.$$

$$\left.\left.\times\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\right\}^{-1}\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\right.$$

$$\times\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left\{\left[\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right.\right.$$

$$\left.\times\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right]\mu_1$$

$$\left.\left.-\left[\left(\rho_1\tau\gamma+\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)-\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\right]\mu_2\right\}\right\}$$

$$=\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)\right.\right.$$

$$\left.-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right.$$

$$\left.\left.\times\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\right\}^{-1}\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\right.$$

$$\times\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left\{\left[\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right.\right.$$

$$\left.\times\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\mu_1$$

$$\left.\left.-\left[\left(\rho_1\tau\gamma+\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}\right)\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)-\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\right]\mu_2\right\}\right\}$$

$$=\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\right.\right.$$

$$\left.-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\right.$$

$$\left.\left.\times\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\right\}^{-1}\left\{\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\right.$$

$$\times\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}$$

$$\left.\times\left[\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\mu_2\right\}$$

$$=\mu_2$$

综上所述，$\hat{\boldsymbol{\mu}}_{ML}$ 对于 $\boldsymbol{\mu}$ 是无偏的。

4. 均值效应量极大似然估计量的协方差矩阵

假设所有的研究都提供所有的均值效应。由多变量统计学的大数定理，合并效应量均值估计量可以近似为一个多元正态分布，其对应的协方差矩阵可由下面的定理给出：

定理 4.1：设效应量设效应量 $\boldsymbol{D}_i$ 服从 $N\left(\begin{pmatrix}\mu_1\\ \mu_2\end{pmatrix},\begin{pmatrix}\sigma_{i1}^2 w_{i1}+\tau^2 & \rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma\\ \rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma & \sigma_{i2}^2 w_{i2}+\gamma^2\end{pmatrix}\right)$ 的正态分布，其极大似然估计量为：$\hat{\boldsymbol{\mu}}_{ML}=\left[\sum_{i=1}^{k}(\boldsymbol{S}_i+\Sigma)^{-1}\right]^{-1}\sum_{i=1}^{k}(\boldsymbol{S}_i+\Sigma)^{-1}\boldsymbol{D}_i$，则 $\hat{\mu}_{ML}$ 所对应的协方差矩阵 $Var\left(\hat{\boldsymbol{\mu}}_{ML}\right)$ 为：

$$Var\left(\hat{\boldsymbol{\mu}}_{ML}\right)_{(1,1)}=\left\{det\left[\sum_{i=1}^{k}(\boldsymbol{S}_i+\Sigma)^{-1}\right]\right\}^{-1}\left\{\sum_{i=1}^{k}det\left[(\boldsymbol{S}_i+\Sigma)\right]^{-1}\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\right\},$$

$$Var\left(\hat{\boldsymbol{\mu}}_{ML}\right)_{(1,2)}=\left\{det\left[\sum_{i=1}^{k}(\boldsymbol{S}_i+\Sigma)^{-1}\right]\right\}^{-1}\left\{\sum_{i=1}^{k}det\left[(\boldsymbol{S}_i+\Sigma)\right]^{-1}\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right\},$$

$$Var\left(\hat{\boldsymbol{\mu}}_{ML}\right)_{(2,1)}=\left\{det\left[\sum_{i=1}^{k}(\boldsymbol{S}_i+\Sigma)^{-1}\right]\right\}^{-1}\left\{\sum_{i=1}^{k}det\left[(\boldsymbol{S}_i+\Sigma)\right]^{-1}\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right\},$$

$$Var\left(\hat{\boldsymbol{\mu}}_{ML}\right)_{(2,2)}=\left\{det\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]\right\}^{-1}\left\{\sum_{i=1}^{k}det\left[\left(\boldsymbol{S}_i+\Sigma\right)\right]^{-1}\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)\right\}。$$

其中 $Var\left(\hat{\boldsymbol{\mu}}_{ML}\right)_{(i,j)}$ 表示矩阵 $Var\left(\hat{\boldsymbol{\mu}}_{ML}\right)$ 第 i 行第 j 列的分量，

$$\begin{aligned}&det\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]\\&=\sum_{i=1}^{k}\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\\&\times\left[\left(\sigma_{j1}^2\omega_{j1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)^2\right]^{-1}\\&\times\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{j2}^2\omega_{j2}+\gamma^2\right)-\left(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma\right)\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)\right]\end{aligned}$$

$$det\left[\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]=\sum_{j=1}^{k}\left[\left(\sigma_{i1}^2\omega_{i1}+\tau^2\right)\left(\sigma_{i2}^2\omega_{i2}+\gamma^2\right)-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma\right)^2\right]。$$

证明：根据多元随机变量的知识可知：如果随机变量 $\boldsymbol{D}\sim N\left(\boldsymbol{\mu},\hat{\Sigma}\right)$，则 $Var\left(\boldsymbol{MD}\right)=\boldsymbol{M}\hat{\Sigma}\boldsymbol{M}^{\mathrm{T}}$，其中 T 表示矩阵的转置。由 $\boldsymbol{S}_i=\boldsymbol{S}_i^{\mathrm{T}}$ 且 $\Sigma^{\mathrm{T}}=\Sigma$，通过计算可得：$\left(\boldsymbol{S}_i+\Sigma\right)^{-1}=\left[\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{\mathrm{T}}$，

$\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{-1}=\left\{\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{-1}\right\}^{\mathrm{T}}$。则

$$\begin{aligned}Var\left(\hat{\boldsymbol{\mu}}_{ML}\right)&=Var\left\{\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{-1}\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}D_i\right\}\\&=Var\left\{\sum_{i=1}^{k}\left\{\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{-1}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}D_i\right\}\right\}\\&=\sum_{i=1}^{k}Var\left\{\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{-1}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}D_i\right\}\\&=\sum_{i=1}^{k}\left\{\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{-1}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\left(\boldsymbol{S}_i+\Sigma\right)\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right\}^{\mathrm{T}}\left\{\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{-1}\right\}^{\mathrm{T}}\\&=\sum_{i=1}^{k}\left\{\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{-1}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\left(\boldsymbol{S}_i+\Sigma\right)\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{-1}\right\}\\&=\sum_{i=1}^{k}\left\{\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{-1}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{-1}\right\}\\&=\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{-1}\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{-1}\\&=\left[\sum_{i=1}^{k}\left(\boldsymbol{S}_i+\Sigma\right)^{-1}\right]^{-1}\end{aligned}$$

因为 $\left(\boldsymbol{S}_i+\Sigma\right)^{-1}=\left[det\left(\boldsymbol{S}_i+\Sigma\right)\right]^{-1}\begin{pmatrix}\sigma_{i2}^2w_{i2}+\gamma^2 & -\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma\right)\\-\left(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma\right) & \sigma_{i1}^2w_{i1}+\tau^2\end{pmatrix}$，

其中 $det(\boldsymbol{S}_i+\Sigma)=(\sigma_{i1}^2 w_{i1}+\tau^2)(\sigma_{i2}^2 w_{i2}+\gamma^2)-(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma)^2$，可得 $\hat{\boldsymbol{\mu}}_{ML}$ 所对应的协方差矩阵 $Var(\hat{\boldsymbol{\mu}}_{ML})$ 为：

$$Var(\hat{\boldsymbol{\mu}}_{ML})_{(1,1)}=\left\{det\left[\sum_{i=1}^{k}(\boldsymbol{S}_i+\Sigma)^{-1}\right]\right\}^{-1}\left\{\sum_{i=1}^{k}det\left[(\boldsymbol{S}_i+\Sigma)\right]^{-1}(\sigma_{i1}^2\omega_{i1}+\tau^2)\right\},$$

$$Var(\hat{\boldsymbol{\mu}}_{ML})_{(1,2)}=\left\{det\left[\sum_{i=1}^{k}(\boldsymbol{S}_i+\Sigma)^{-1}\right]\right\}^{-1}\left\{\sum_{i=1}^{k}det\left[(\boldsymbol{S}_i+\Sigma)\right]^{-1}(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma)\right\},$$

$$Var(\hat{\boldsymbol{\mu}}_{ML})_{(2,1)}=\left\{det\left[\sum_{i=1}^{k}(\boldsymbol{S}_i+\Sigma)^{-1}\right]\right\}^{-1}\left\{\sum_{i=1}^{k}det\left[(\boldsymbol{S}_i+\Sigma)\right]^{-1}(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma)\right\},$$

$$Var(\hat{\boldsymbol{\mu}}_{ML})_{(2,2)}=\left\{det\left[\sum_{i=1}^{k}(\boldsymbol{S}_i+\Sigma)^{-1}\right]\right\}^{-1}\left\{\sum_{i=1}^{k}det\left[(\boldsymbol{S}_i+\Sigma)\right]^{-1}(\sigma_{i2}^2\omega_{i2}+\gamma^2)\right\}。$$

其中

$$\begin{aligned}&det\left[\sum_{i=1}^{k}(\boldsymbol{S}_i+\Sigma)^{-1}\right]\\&=\sum_{i=1}^{k}\sum_{j=1}^{k}\left[(\sigma_{i1}^2\omega_{i1}+\tau^2)(\sigma_{i2}^2\omega_{i2}+\gamma^2)-(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma)^2\right]^{-1}\\&\times\left[(\sigma_{j1}^2\omega_{j1}+\tau^2)(\sigma_{j2}^2\omega_{j2}+\gamma^2)-(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma)^2\right]^{-1}\\&\times\left[(\sigma_{i1}^2\omega_{i1}+\tau^2)(\sigma_{j2}^2\omega_{j2}+\gamma^2)-(\rho_0\sigma_{j1}\sigma_{j2}\sqrt{\omega_{j1}\omega_{j2}}+\rho_1\tau\gamma)(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma)\right]\end{aligned}$$

$$det\left[(\boldsymbol{S}_i+\Sigma)^{-1}\right]=\sum_{j=1}^{k}\left[(\sigma_{i1}^2\omega_{i1}+\tau^2)(\sigma_{i2}^2\omega_{i2}+\gamma^2)-(\rho_0\sigma_{i1}\sigma_{i2}\sqrt{\omega_{i1}\omega_{i2}}+\rho_1\tau\gamma)^2\right]。$$

通过 $\hat{\boldsymbol{\mu}}_{ML}$ 所对应的协方差矩阵 $Var(\hat{\boldsymbol{\mu}}_{ML})$ 可以给出单变量和联合变量的置信区域，其具体形式为：

性质 3.1：设效应量设效应量 $\boldsymbol{D}_i$ 服从 $N\left(\begin{pmatrix}\mu_1\\ \mu_2\end{pmatrix},\begin{pmatrix}\sigma_{i1}^2 w_{i1}+\tau^2 & \rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma\\ \rho_0\sigma_{i1}\sigma_{i2}\sqrt{w_{i1}w_{i2}}+\rho_1\tau\gamma & \sigma_{i2}^2 w_{i2}+\gamma^2\end{pmatrix}\right)$ 的正态分布，其极大似然估计量为：$\hat{\boldsymbol{\mu}}_{ML}=\left[\sum_{i=1}^{k}(\boldsymbol{S}_i+\Sigma)^{-1}\right]^{-1}\sum_{i=1}^{k}(\boldsymbol{S}_i+\Sigma)^{-1}\boldsymbol{D}_i$，则合并均值效应量 $\hat{\boldsymbol{\mu}}_{ML}$ 所对应各个分量的 $(1-\alpha)100\%$ 置信区间为：

$\left(\hat{\mu}_1-Z_{\frac{\alpha}{2}}\sqrt{Var(\hat{\boldsymbol{\mu}}_{ML})_{(1,1)}},\hat{\mu}_1+Z_{\frac{\alpha}{2}}\sqrt{Var(\hat{\boldsymbol{\mu}}_{ML})_{(1,1)}}\right)$ 和 $\left(\hat{\mu}_2-Z_{\frac{\alpha}{2}}\sqrt{Var(\hat{\boldsymbol{\mu}}_{ML})_{(2,2)}},\hat{\mu}_2+Z_{\frac{\alpha}{2}}\sqrt{Var(\hat{\boldsymbol{\mu}}_{ML})_{(2,2)}}\right)$，其中 $Z_{\frac{\alpha}{2}}$ 表示正态分布的 $\frac{\alpha}{2}$ 分位数，$Var(\hat{\boldsymbol{\mu}}_{ML})_{(i,j)}$ 表示矩阵 $Var(\hat{\boldsymbol{\mu}}_{ML})$ 第 i 行第 j 列的分量。

5. 结束语

本文给出已知协方差矩阵的基于均差估值的二变量 Meta-分析随机效应模型，并通过极大似然估计法给出效应量估计。通过计算估计效应量的协方差矩阵，给出效应分量的 $(1-\alpha)100\%$ 置信区间。这些结论对临床医学，特别是流行病学会有较好的统计学和现实意义。

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