



ANATOMÍA Y FISIOLOGÍA DEL NETWORK META-ANALYSIS

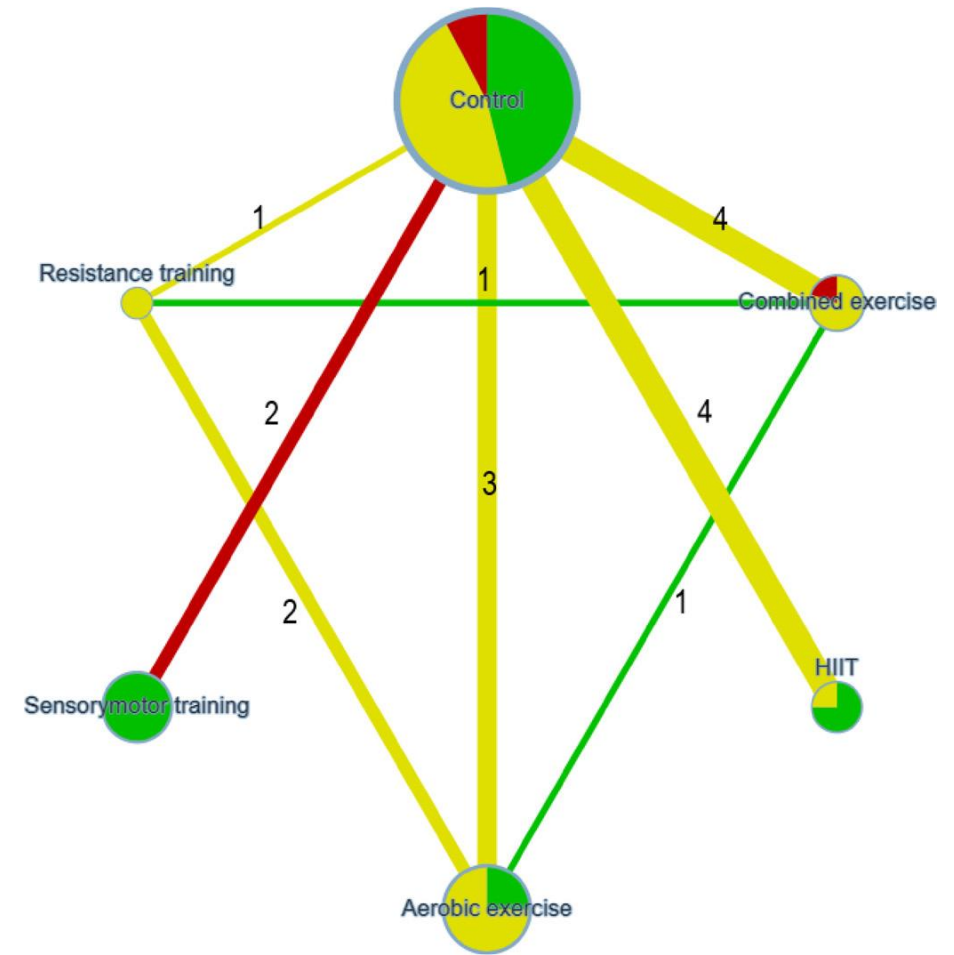
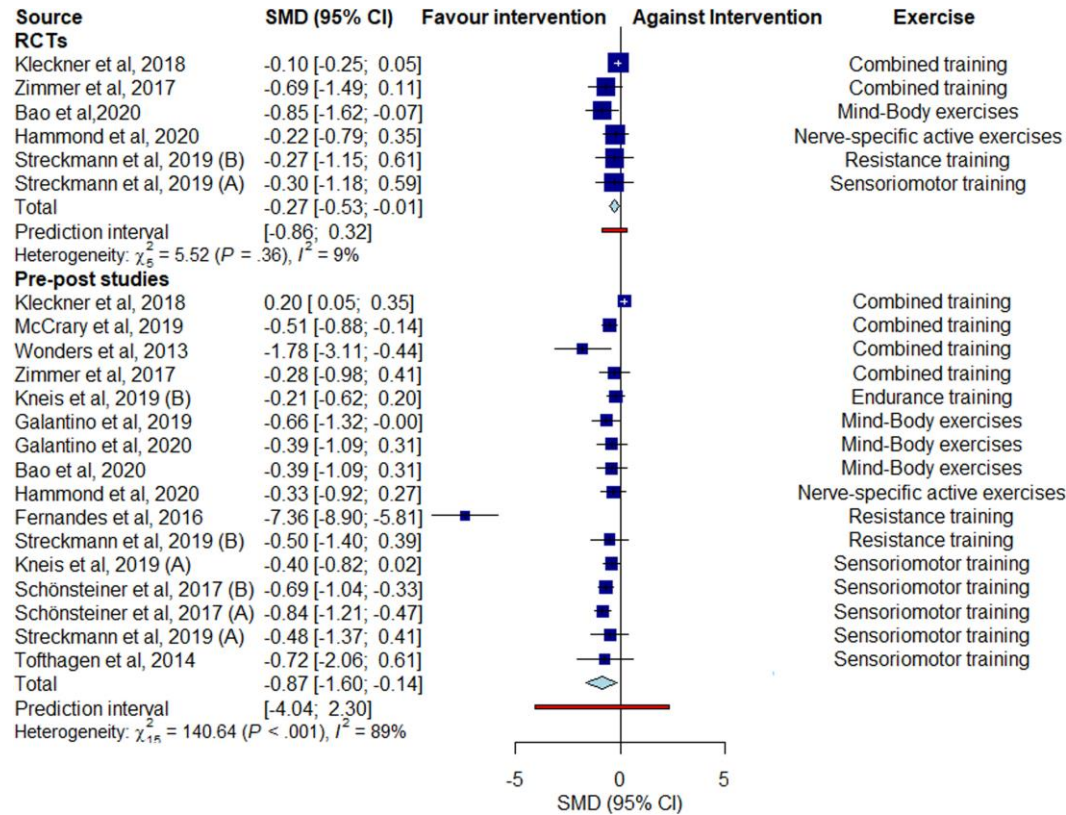
Sergio Núñez de Arenas Arroyo
Sergio.NunezdeArenas@uclm.es

2-noviembre-2023

Índice

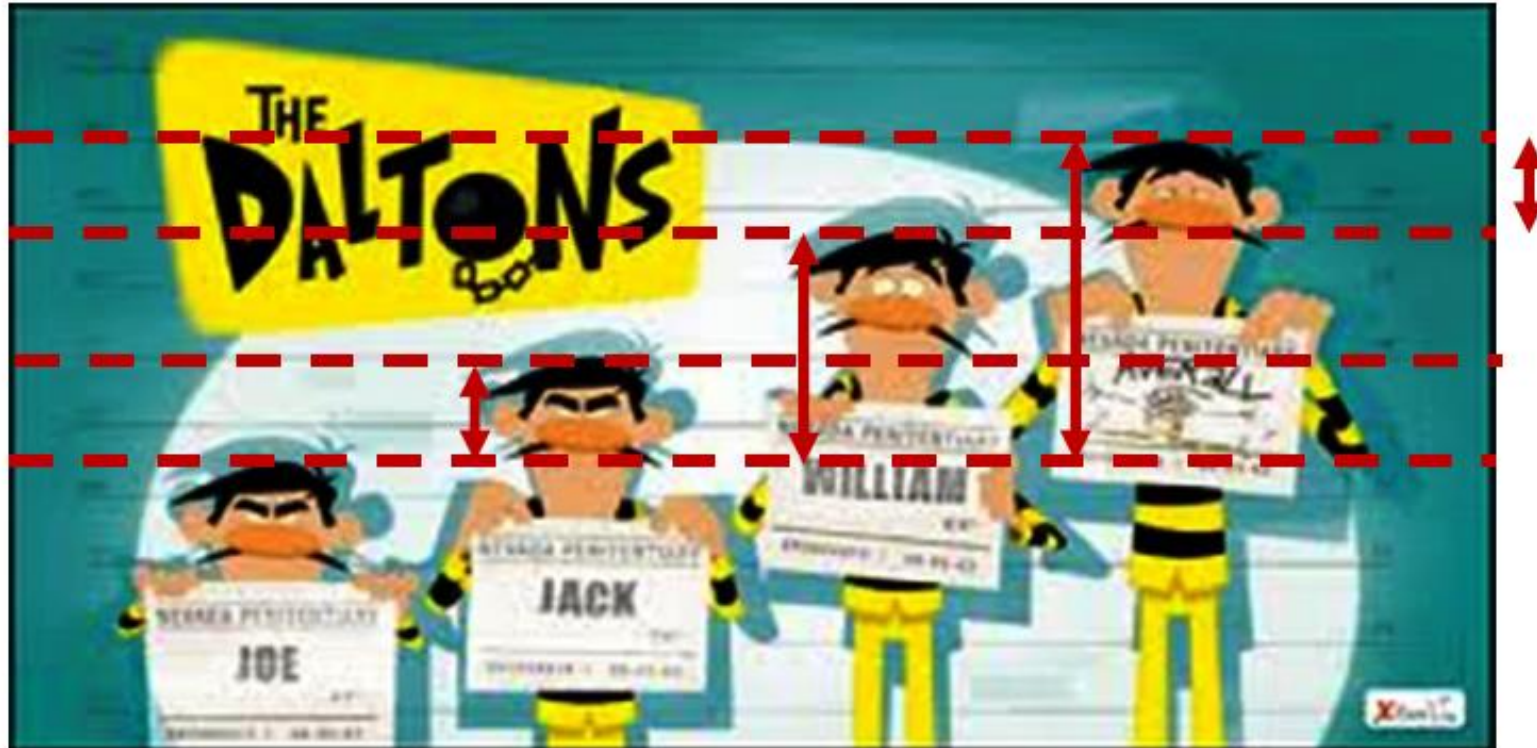
1. ¿Qué es un Network meta-analysis (NMA)?
2. Evidencia directa vs evidencia indirecta
3. Órganos clave: transitividad y consistencia
4. Interpretación de un NMA
5. Component-NMA (CNMA)

¿Qué es un NMA?

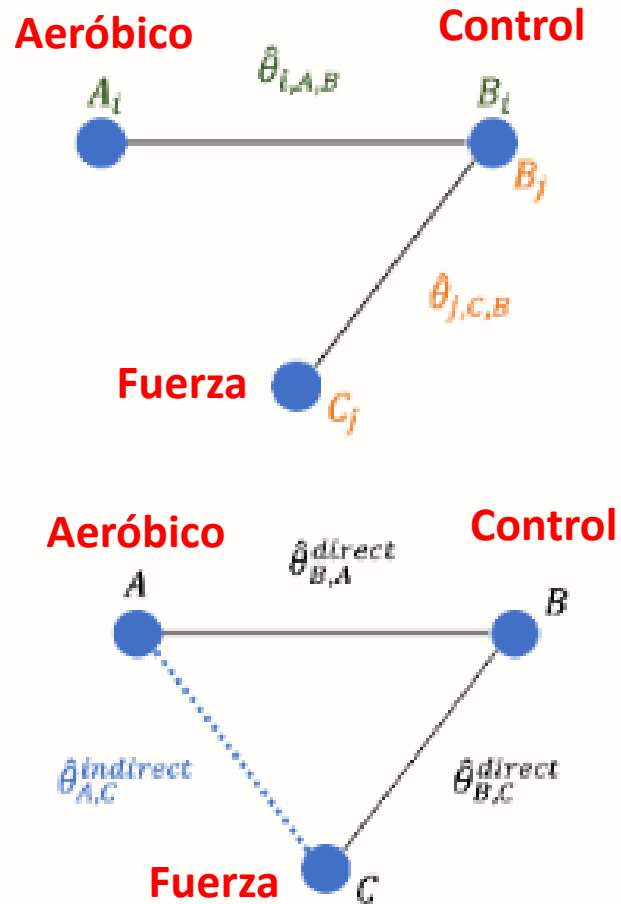


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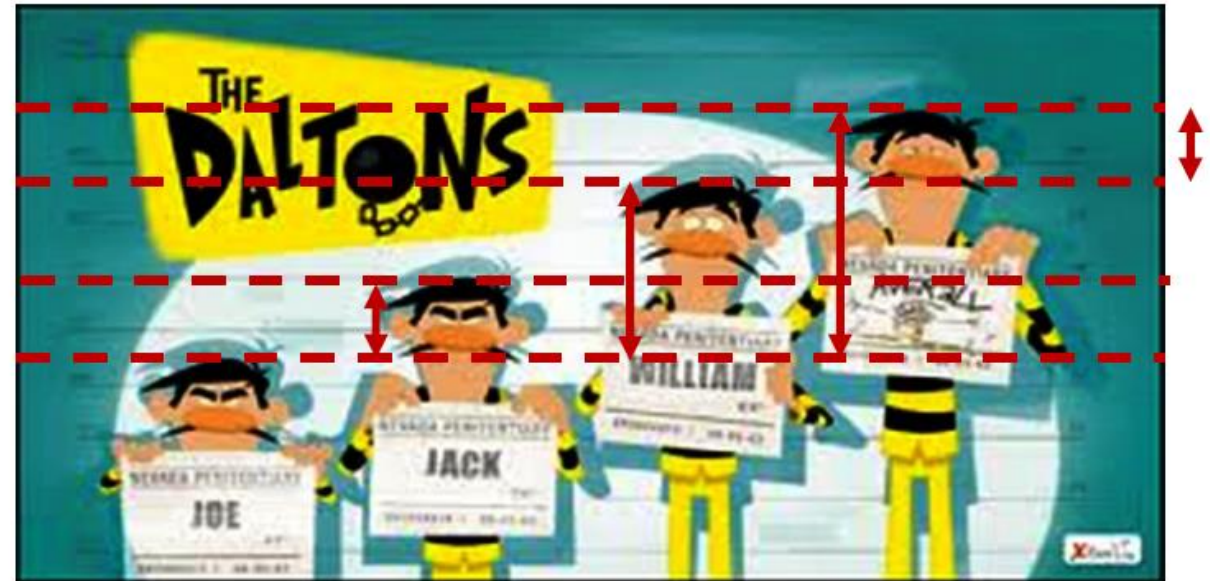
- If we know how much taller is Averail to Joe and how much taller is William to Joe, we know how much taller is Averail to William



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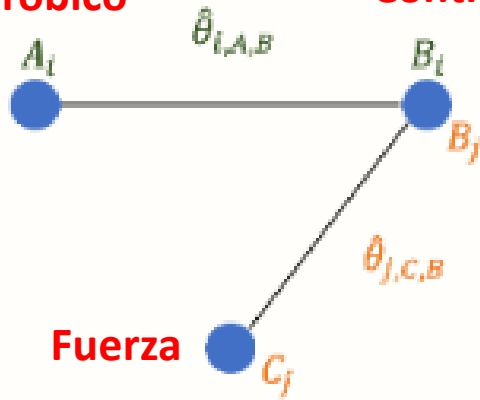
Control

Aeróbico **Fuerza**



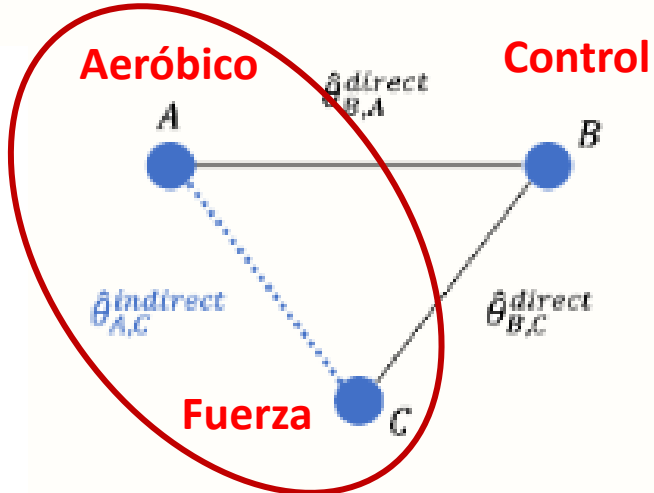
¿Qué es un NMA?

Aeróbico **Control**



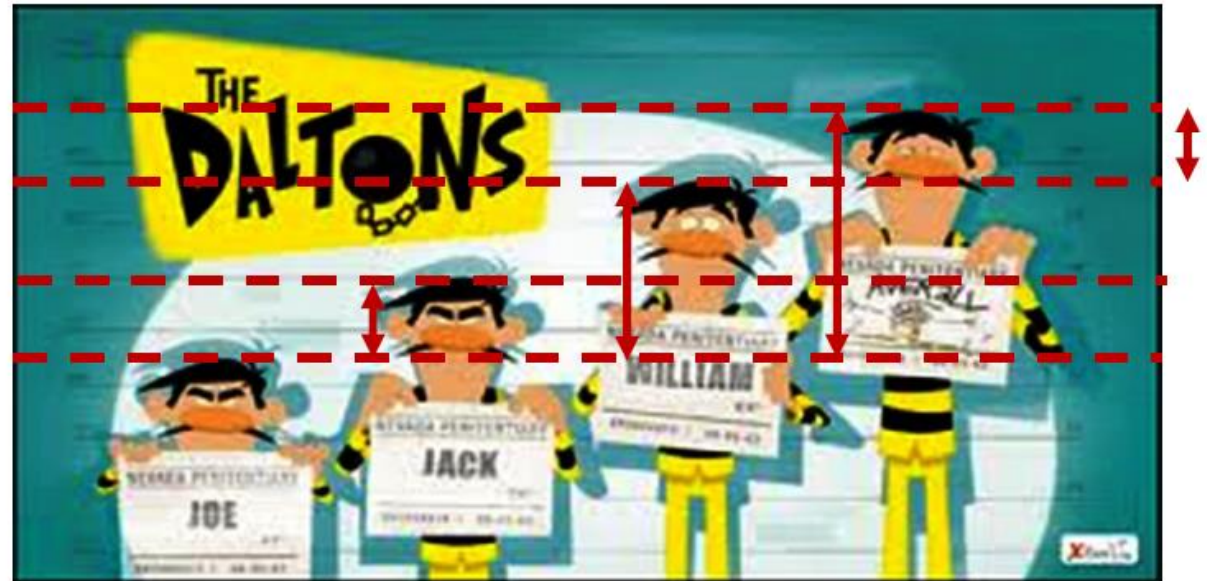
Fuerza

Aeróbico **Control**



Fuerza

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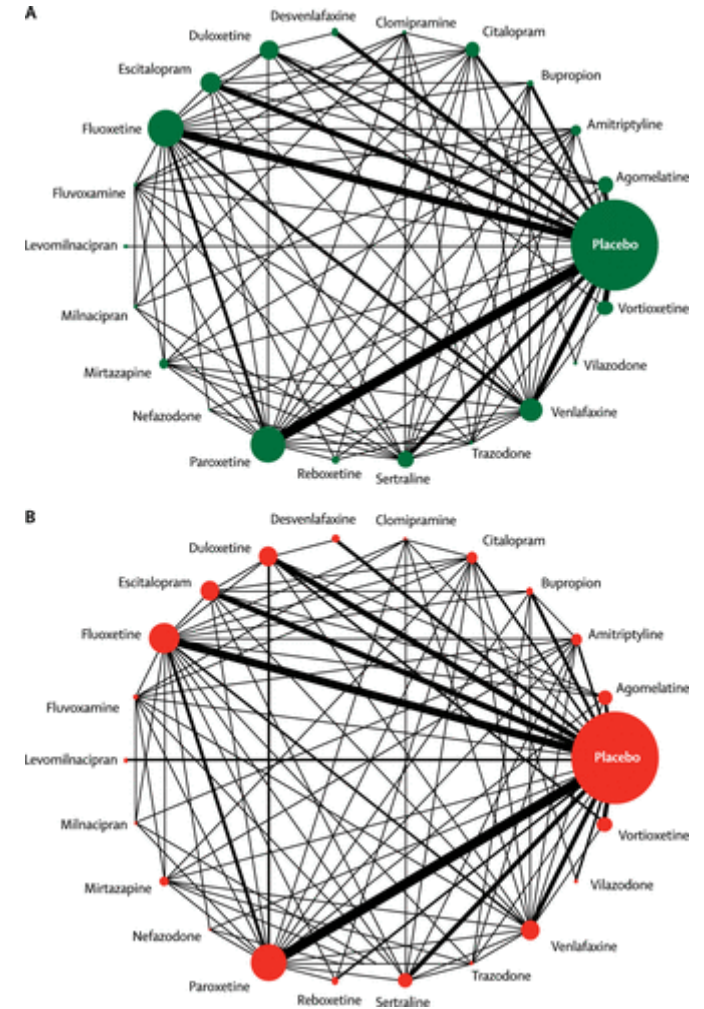
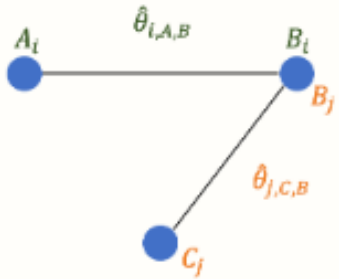
Control

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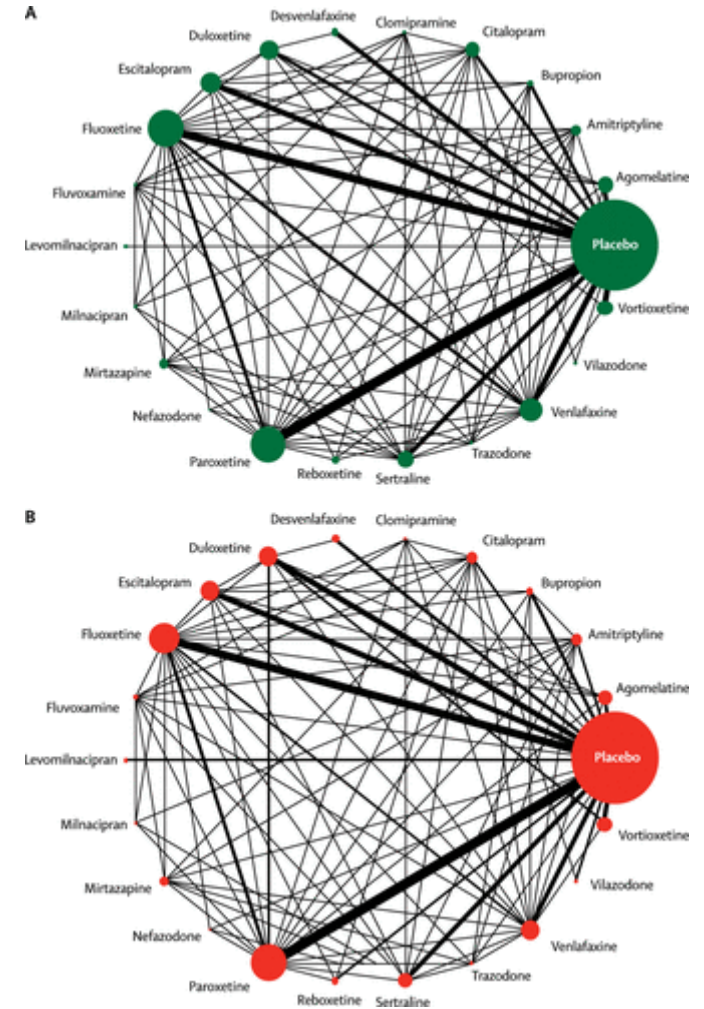
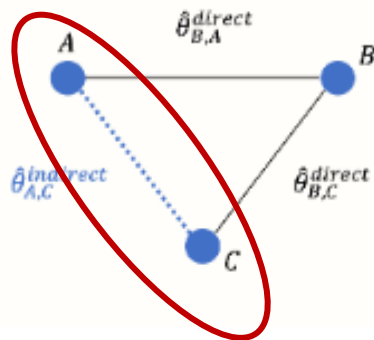
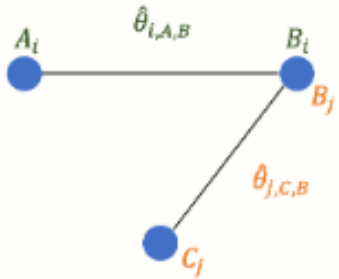
Evidencia directa vs indirecta

| Evidencia directa | Evidencia indirecta | Evidencia del NMA |
|--------------------------|--|---|
| Comparaciones existentes | Resultado procedente de las relaciones con otros nodos | Combinación de las dos anteriores  |



Evidencia directa vs indirecta

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Ventajas del NMA sobre MA

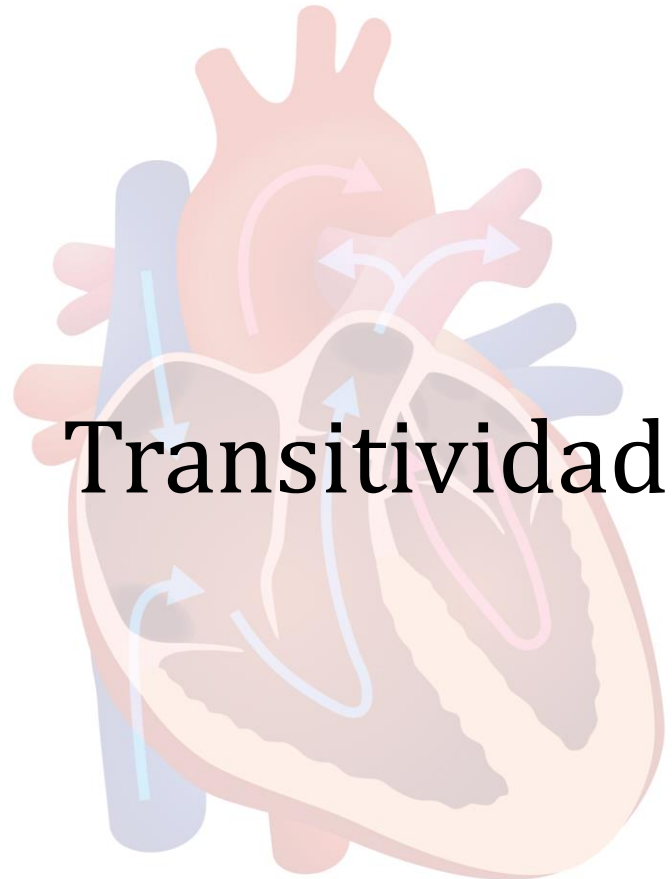
- Estima efectos entre intervenciones no comparadas.
- ↑ Precisión (combina evidencia directa e indirecta).
- Reúne toda la información disponible de un conjunto de estudios relacionados en un solo análisis (más utilidad clínica).
- MA por pares para mostrar solo la evidencia directa.
- Inferir que tipo de tratamiento puede ser preferible para la población de estudio (ranking)

Pero...

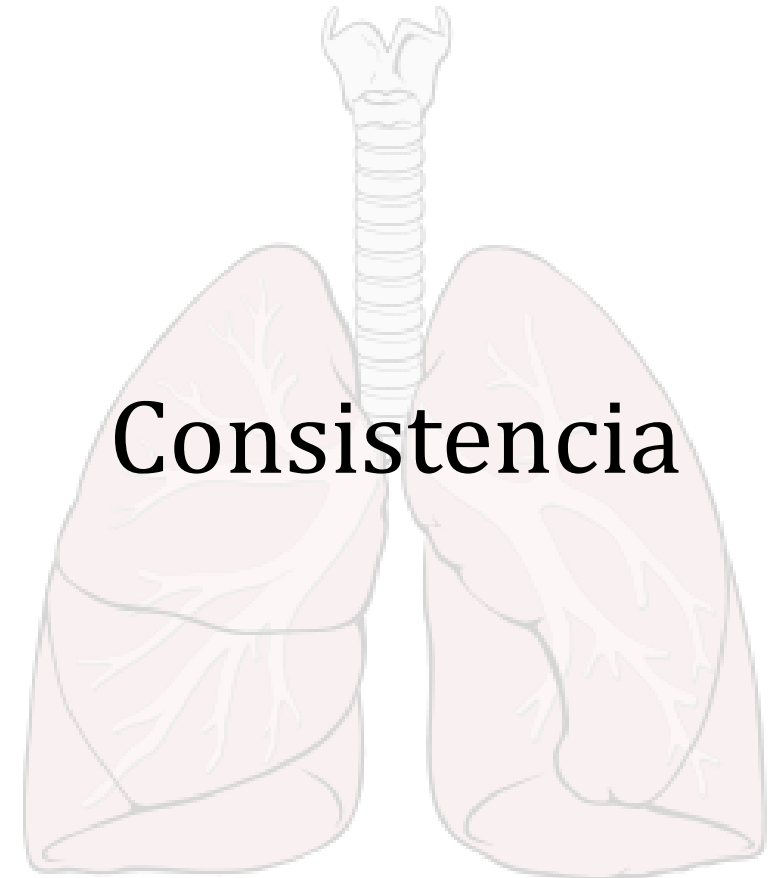
¿Está justificado el uso de la evidencia indirecta, sobre todo en los casos donde existe evidencia directa?



Órganos clave del NMA

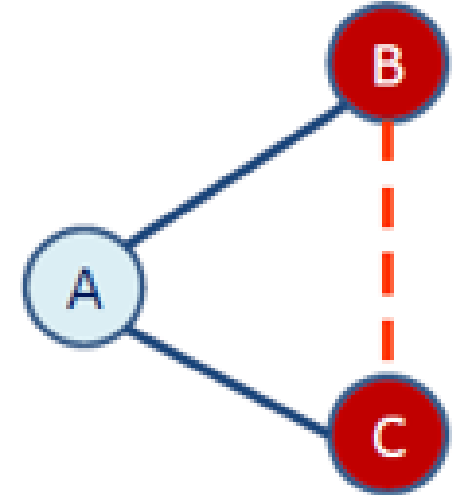


NMA



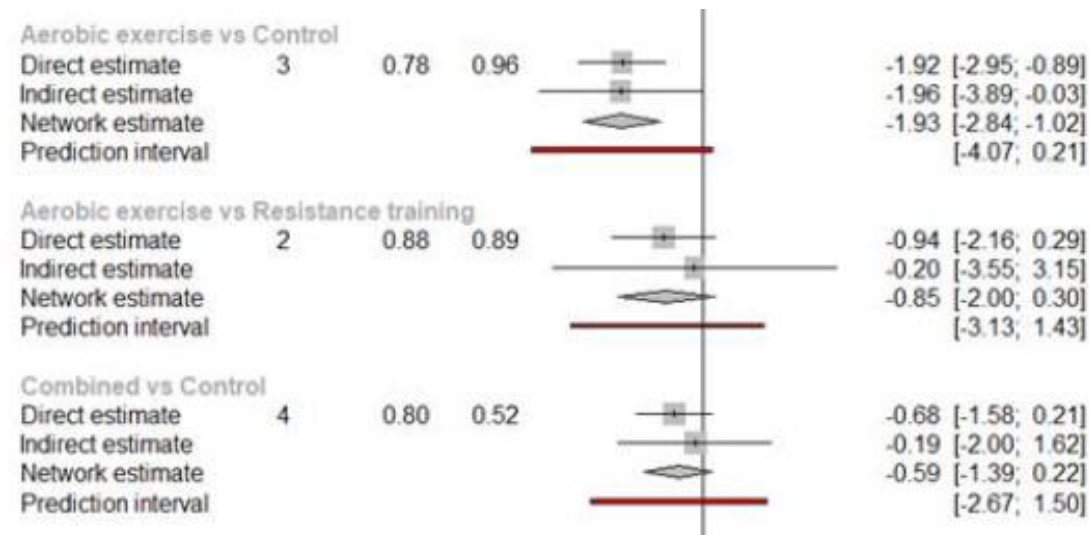
Transitividad

1. Tratamiento A es igual cuando se compara AB que cuando se compara AC.
2. Los participantes incluidos en la red podrían haber sido randomizados/asignados a cualquiera de los tratamientos.
3. Los estudios incluidos no difieren en relación a las variables modificadoras del efecto (severidad, estadio, edad...).



Consistencia

1. Manifestación estadística de la transitividad.
2. Se define como la coherencia entre la evidencia directa y la evidencia indirecta.



Por tanto...

¿Está justificado el uso de la evidencia indirecta, sobre todo en los casos donde existe evidencia directa?



Por tanto...

¿Está justificado el uso de la evidencia indirecta, sobre todo en los casos donde existe evidencia directa?



La evidencia del NMA será más precisa siempre que se cumplan los supuestos de transitividad y consistencia

INTERPRETACIÓN DE LOS RESULTADOS DE UN NETWORK META-ANÁLISIS

Systematic review

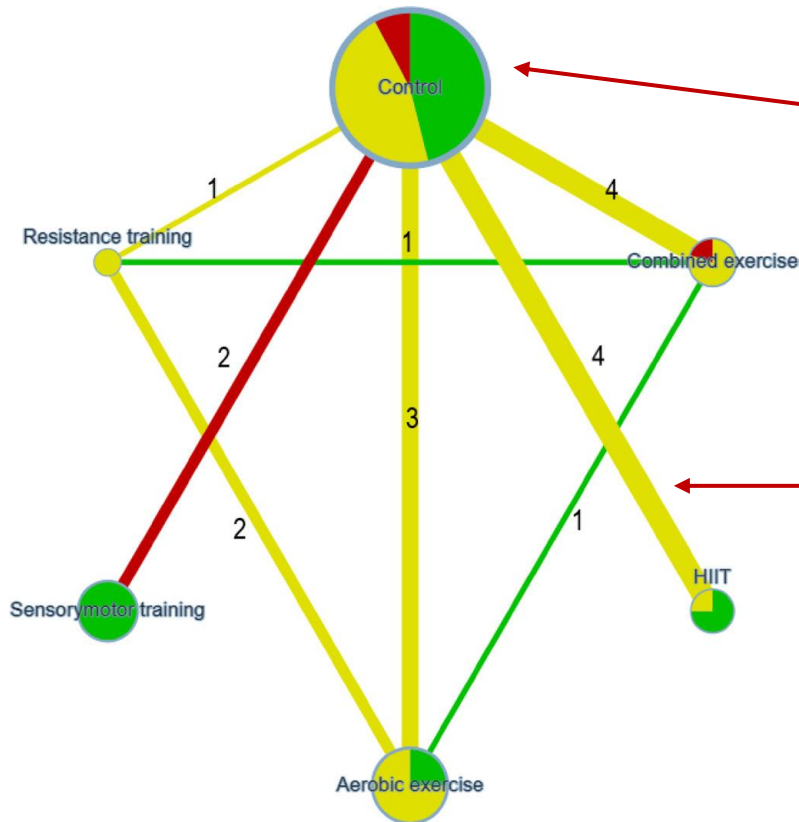
Comparative effectiveness of different types of exercise in reducing arterial stiffness in children and adolescents: a systematic review and network meta-analysis

Irene Sequi-Dominguez ^{1,2} Dimitris Mavridis,^{3,4} Iván Cervero-Redondo ⁵
Alicia Saz-Lara ¹ Vicente Martínez-Vizcaino ¹
Sergio Núñez de Arenas-Arroyo ¹



Our objective was to compare the effectiveness of different types of exercise in reducing arterial stiffness in children and adolescents

Network plot



Nodos: Número de participantes o número de estudios con esa intervención.

Líneas: Número de estudios con esa comparación

Colores: CINEMA software

League table

Table S4. Pooled SMD on types of PE. Upper right triangle gives the pooled mean differences from pairwise comparisons, lower left triangle pooled mean differences from the network meta-analysis (row intervention relative to column).

| | | | | | |
|----------------------|---------------------|----------------------|---------------------|-----------------------|----------------------|
| Aerobic exercise | -1.36 (-3.08; 0.36) | NA | -0.94 (-2.16; 0.29) | NA | -1.92 (-2.95; -0.89) |
| -1.34 (-2.41; -0.28) | Combined | NA | 1.00 (-0.71; 2.71) | NA | -0.68 (-1.58; 0.21) |
| -0.82 (-2.10; 0.46) | 0.52 (-0.69; 1.73) | HIIT | NA | NA | -1.11 (-2.01; -0.21) |
| -0.85 (-2.00; 0.30) | 0.49 (-0.76; 1.74) | -0.03 (-1.53; 1.46) | Resistance training | NA | -0.73 (-2.50; 1.04) |
| -2.04 (-3.55; -0.53) | -0.70 (-2.15; 0.75) | -1.22 (-2.73; 0.29) | -1.19 (-2.88; 0.51) | Sensorymotor training | 0.11 (-1.10; 1.32) |
| -1.93 (-2.84; -1.02) | -0.59 (-1.39; 0.22) | -1.11 (-2.01; -0.21) | -1.08 (-2.27; 0.11) | 0.11 (-1.10; 1.32) | Control |

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Evidencia directa

Comparaciones no existentes

Evidencia del NMA

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Evidencia directa

Comparaciones no existentes

Evidencia del NMA

Tabla resultados

Table 1 Pooled SMD with 95% CI, P-scores and Confidence in Network Meta-Analysis confidence ratings for the exercise interventions

| Type of exercise intervention | Studies (n) | Participants (n) | Effect size (95% CI) | | P value | 95% PI | P-score |
|-------------------------------|-------------|------------------|----------------------|----------------------|---------|-------------|---------|
| | | | Direct estimate | NMA estimate | | | |
| Aerobic exercise | 3 | 258 | -2.02 (-3.89, 0.15) | -1.93 (-2.84, -1.02) | < 0.000 | -4.07; 0.22 | 0.96 |
| Combined | 4 | 138 | -0.71 (-1.22, 0.20) | -0.59 (-1.39, 0.22) | 0.15 | -2.67; 1.50 | 0.44 |
| HIIT | 4 | 205 | -1.09 (-1.88, 0.29) | -1.11 (-2.01, -0.21) | 0.02 | -3.25; 1.03 | 0.67 |
| Resistance training | 1 | 39 | -0.73 (-1.38, 0.08) | -1.08 (-2.27, 0.11) | 0.07 | -3.39; 1.23 | 0.64 |
| Sensorimotor training | 2 | 203 | 0.08 (-0.22, 0.37) | 0.11 (-1.10, 1.32) | 0.86 | -2.21; 2.43 | 0.15 |

HIIT, high intensity interval training; NMA, network meta-analysis; SMD, standardised mean difference.

Pero...

| | | | | | | | | | | | | | | | | | | | | | |
|-------|------|------|------|------|------|------|------|-------|-------|------|------|------|------|------|------|------|------|-------|------|------|-----|
| PHE | 0.22 | 0.49 | 0.54 | 0.63 | 0.64 | 0.69 | 0.71 | 0.67 | 0.69 | 0.72 | 0.74 | 0.77 | 0.77 | 0.80 | 0.88 | 0.99 | 1.11 | 1.01 | 1.14 | 1.34 | -- |
| 6.43 | MIR | 0.27 | 0.32 | 0.41 | 0.42 | 0.47 | 0.49 | 0.45 | 0.47 | 0.50 | 0.52 | 0.55 | 0.55 | 0.58 | 0.66 | 0.77 | 0.89 | 0.79 | 0.92 | 1.12 | -- |
| 9.02 | 1.40 | OLA | 0.04 | 0.13 | 0.14 | 0.20 | 0.21 | 0.17 | 0.20 | 0.23 | 0.24 | 0.28 | 0.28 | 0.31 | 0.39 | 0.49 | 0.62 | 0.51 | 0.65 | 0.85 | -- |
| 7.83 | 1.22 | 0.87 | BRO | 0.09 | 0.10 | 0.15 | 0.17 | 0.13 | 0.15 | 0.18 | 0.20 | 0.24 | 0.24 | 0.26 | 0.35 | 0.45 | 0.57 | 0.47 | 0.60 | 0.80 | -- |
| 7.20 | 1.12 | 0.80 | 0.92 | PAR | 0.01 | 0.06 | 0.08 | 0.04 | 0.07 | 0.09 | 0.11 | 0.15 | 0.15 | 0.18 | 0.26 | 0.36 | 0.48 | 0.38 | 0.51 | 0.71 | -- |
| 8.01 | 1.25 | 0.89 | 1.02 | 1.11 | PRZ | 0.05 | 0.07 | 0.03 | 0.05 | 0.08 | 0.10 | 0.14 | 0.14 | 0.16 | 0.25 | 0.35 | 0.47 | 0.37 | 0.50 | 0.70 | -- |
| 6.25 | 0.97 | 0.69 | 0.80 | 0.87 | 0.78 | VEN | 0.02 | -0.02 | 0.00 | 0.03 | 0.04 | 0.08 | 0.08 | 0.11 | 0.19 | 0.30 | 0.42 | 0.32 | 0.45 | 0.65 | -- |
| 5.55 | 0.86 | 0.62 | 0.71 | 0.77 | 0.69 | 0.89 | FLX | -0.04 | -0.01 | 0.01 | 0.03 | 0.07 | 0.07 | 0.10 | 0.18 | 0.28 | 0.40 | 0.30 | 0.43 | 0.63 | -- |
| 11.29 | 1.76 | 1.25 | 1.44 | 1.57 | 1.41 | 1.81 | 2.03 | AMI | 0.03 | 0.05 | 0.07 | 0.11 | 0.11 | 0.14 | 0.22 | 0.32 | 0.45 | 0.34 | 0.48 | 0.67 | -- |
| 4.09 | 0.64 | 0.45 | 0.52 | 0.57 | 0.51 | 0.65 | 0.74 | 0.36 | IMI | 0.03 | 0.04 | 0.08 | 0.08 | 0.11 | 0.19 | 0.30 | 0.42 | 0.31 | 0.45 | 0.65 | -- |
| 11.75 | 1.83 | 1.30 | 1.50 | 1.63 | 1.47 | 1.88 | 2.12 | 1.04 | 2.87 | TPM | 0.02 | 0.06 | 0.06 | 0.08 | 0.17 | 0.27 | 0.39 | 0.29 | 0.42 | 0.62 | -- |
| 12.81 | 1.99 | 1.42 | 1.64 | 1.78 | 1.60 | 2.05 | 2.31 | 1.13 | 3.13 | 1.09 | 0.04 | 0.04 | 0.07 | 0.15 | 0.25 | 0.38 | 0.27 | 0.41 | 0.60 | -- | |
| 10.45 | 1.63 | 1.16 | 1.33 | 1.45 | 1.30 | 1.67 | 1.88 | 0.92 | 2.55 | 0.89 | 0.82 | NEF | 0.00 | 0.03 | 0.11 | 0.21 | 0.34 | 0.23 | 0.37 | -- | |
| 8.32 | 1.29 | 0.92 | 1.06 | 1.16 | 1.04 | 1.33 | 1.50 | 0.74 | 2.03 | 0.71 | 0.65 | 0.80 | SER | 0.03 | 0.11 | 0.21 | 0.34 | 0.23 | 0.37 | -- | |
| 9.04 | 1.41 | 1.00 | 1.15 | 1.26 | 1.13 | 1.45 | 1.63 | 0.80 | 2.21 | 0.77 | 0.71 | 0.86 | 1.09 | NK1R | 0.08 | 0.18 | 0.31 | 0.20 | 0.34 | -- | |
| 12.91 | 2.01 | 1.43 | 1.65 | 1.79 | 1.61 | 2.07 | 2.33 | 1.14 | 3.16 | 1.10 | 1.01 | 1.24 | 1.55 | 1.43 | GUA | 0.10 | 0.23 | 0.12 | 0.26 | -- | |
| 4.68 | 0.73 | 0.60 | 0.65 | 0.58 | 0.75 | 0.84 | 0.41 | 1.14 | 0.40 | 0.37 | 0.45 | 0.56 | 0.52 | 0.36 | 0.52 | 0.36 | TGB | 0.12 | 0.02 | 0.15 | -- |
| 10.00 | 1.56 | 1.11 | 1.28 | 1.39 | 1.25 | 1.60 | 1.80 | 0.89 | 2.44 | 0.85 | 0.78 | 0.96 | 1.20 | 1.11 | 0.77 | 2.14 | BUP | -0.10 | 0.03 | 0.23 | -- |
| 7.50 | 1.17 | 0.83 | 0.96 | 1.04 | 0.94 | 1.20 | 1.35 | 0.66 | 1.83 | 0.64 | 0.59 | 0.72 | 0.90 | 0.83 | 0.58 | 1.60 | 0.75 | PLB | 0.13 | -- | |
| 8.21 | 1.28 | 0.91 | 1.05 | 1.14 | 1.03 | 1.31 | 1.48 | 0.73 | 2.01 | 0.70 | 0.64 | 0.79 | 0.99 | 0.91 | 0.64 | 1.76 | 0.82 | 1.10 | DVP | -- | |
| 5.58 | 0.87 | 0.62 | 0.71 | 0.77 | 0.70 | 0.89 | 1.00 | 0.49 | 1.36 | 0.47 | 0.44 | 0.53 | 0.67 | 0.62 | 0.43 | 1.19 | 0.56 | 0.74 | 0.68 | -- | |
| 0.94 | 0.15 | 0.10 | 0.12 | 0.13 | 0.12 | 0.15 | 0.17 | 0.08 | 0.23 | 0.08 | 0.07 | 0.09 | 0.11 | 0.10 | 0.07 | 0.20 | 0.09 | 0.12 | 0.11 | 0.17 | LAM |



Ranking según jerarquía

- Probability for a treatment of being the best ($P(\text{best})$)
- Rank probabilities
- **Surface under the cumulative ranking (SUCRA) curve**
- **P-score**
- Mean/median rank

Ranking según jerarquía

a hierarchy of exercise interventions, using P-scores.³⁵ P-scores give for each intervention the mean extent of certainty that it is better than all competing interventions; the closer the P-score is to 1 the better the intervention. The probability that each exercise intervention assumes any of the possible ranks was presented graphically using rankograms.³⁶

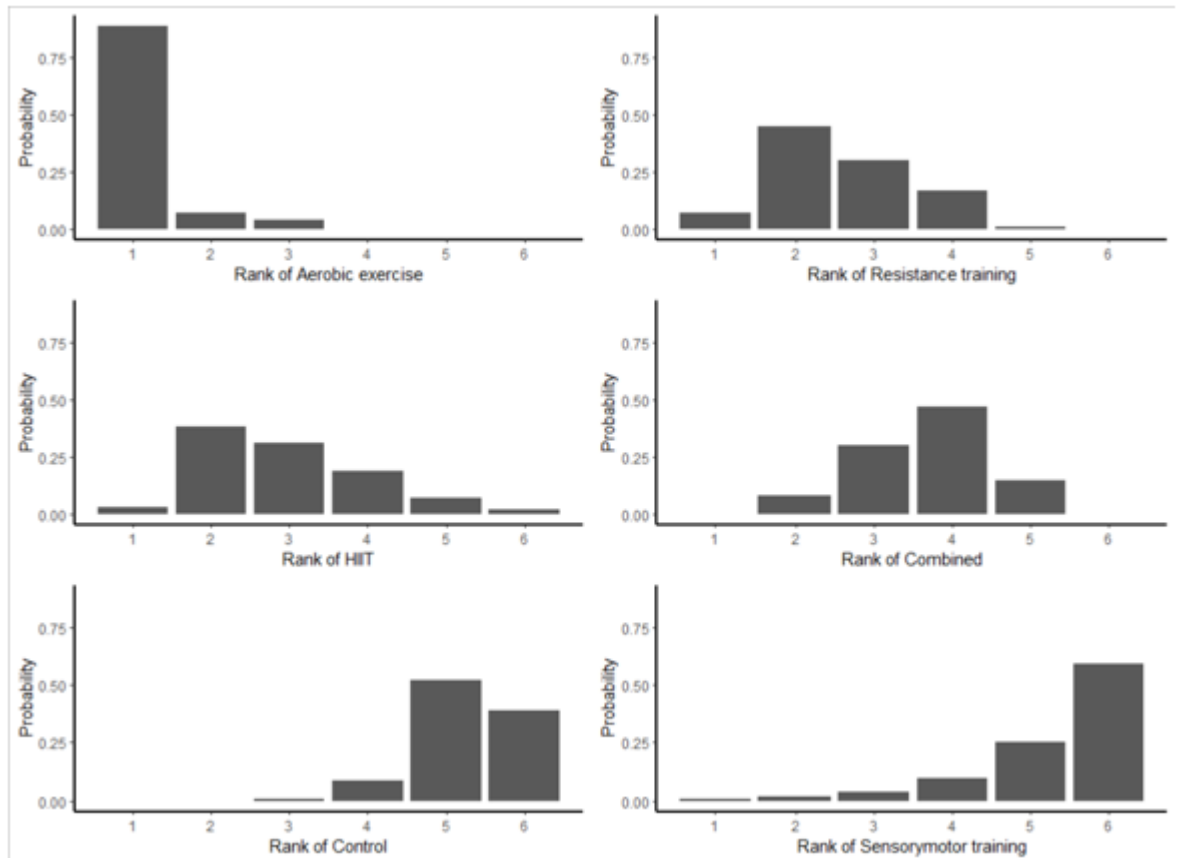
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HIIT, high intensity interval training; NMA, network meta-analysis; SMD, standardised mean difference.

Ranking según jerarquía

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¿Realmente puedo decir que el ejercicio aeróbico es superior al resto de ejercicios?

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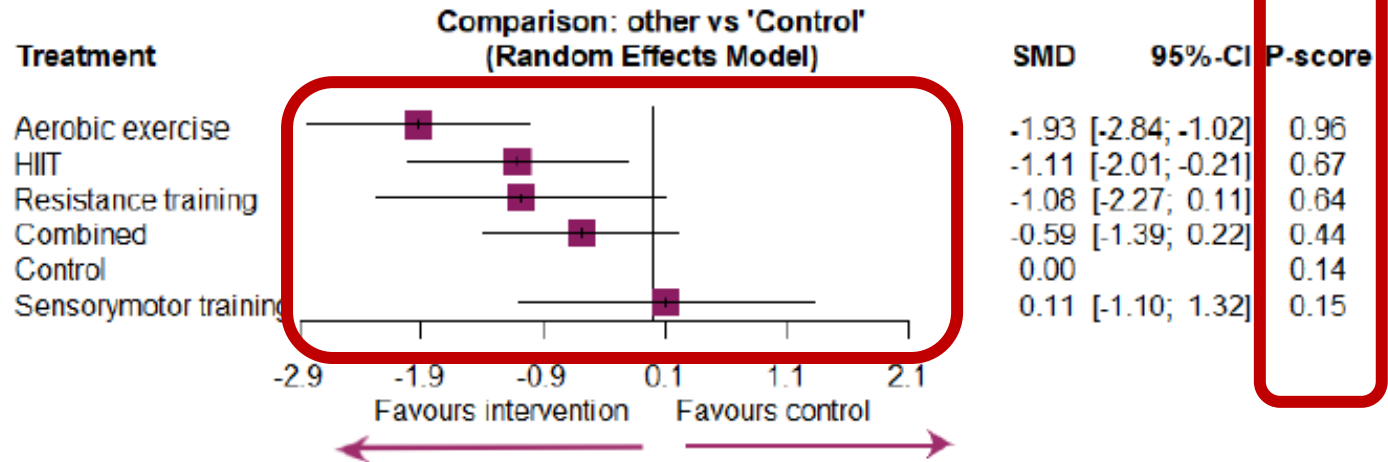


Figure S2. Forest plot of the pooled effect of each modality of exercise compared to the control group

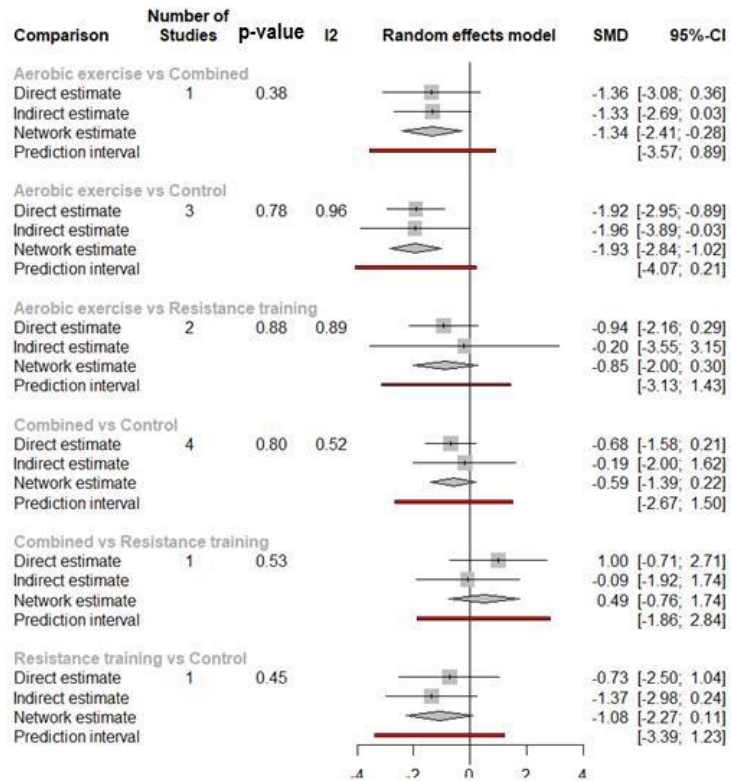
Valoración de la inconsistencia

1. Local (node-splitting)
2. Global (estadístico Q)

Valoración de la inconsistencia

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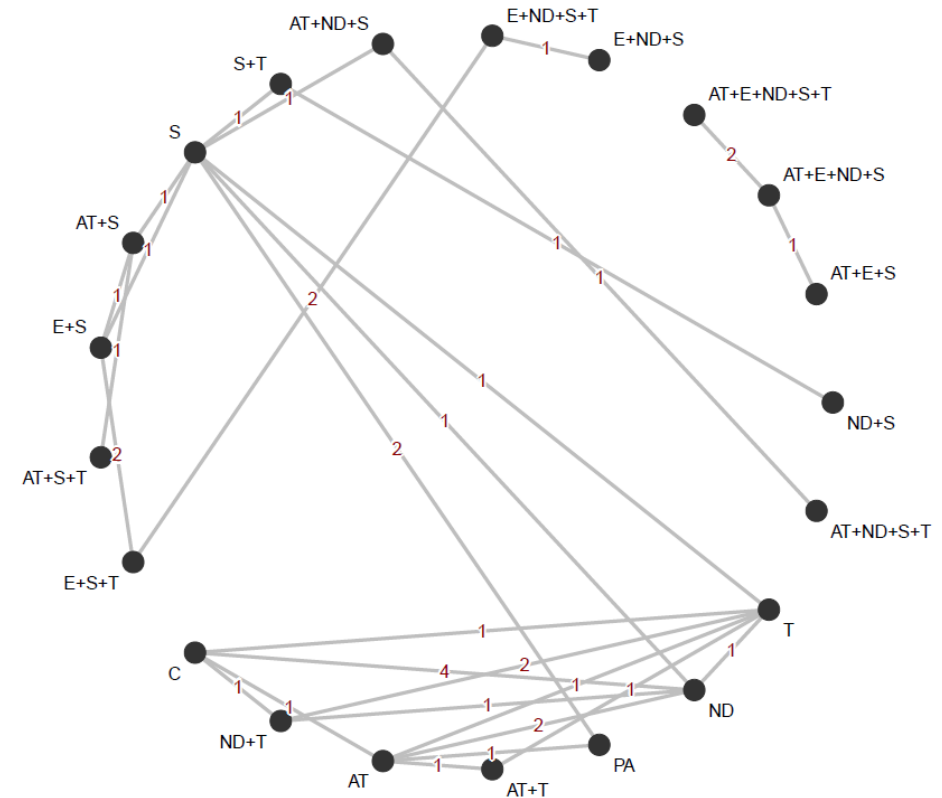
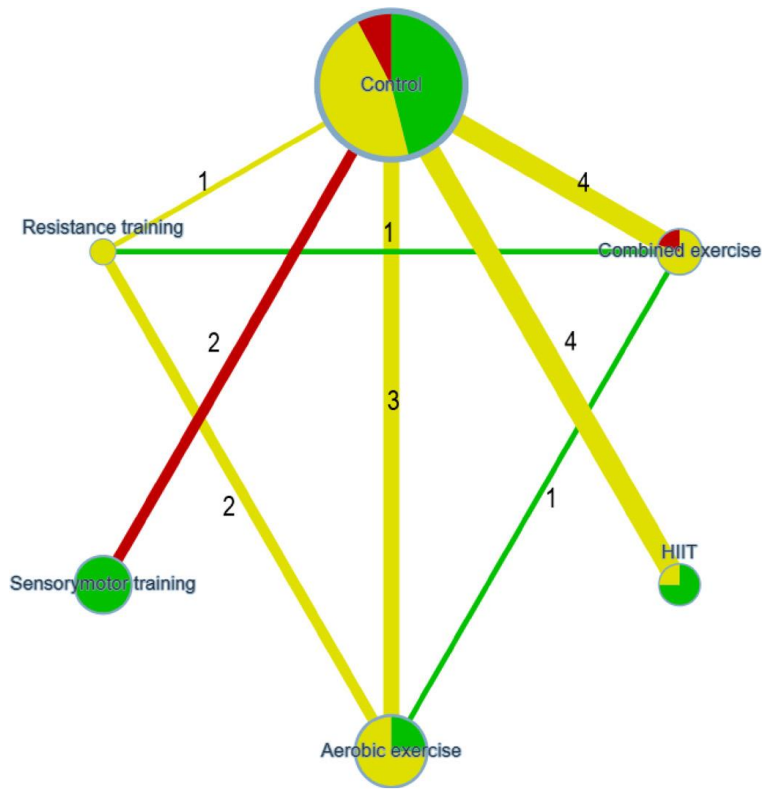
2. Global (estadístico Q)



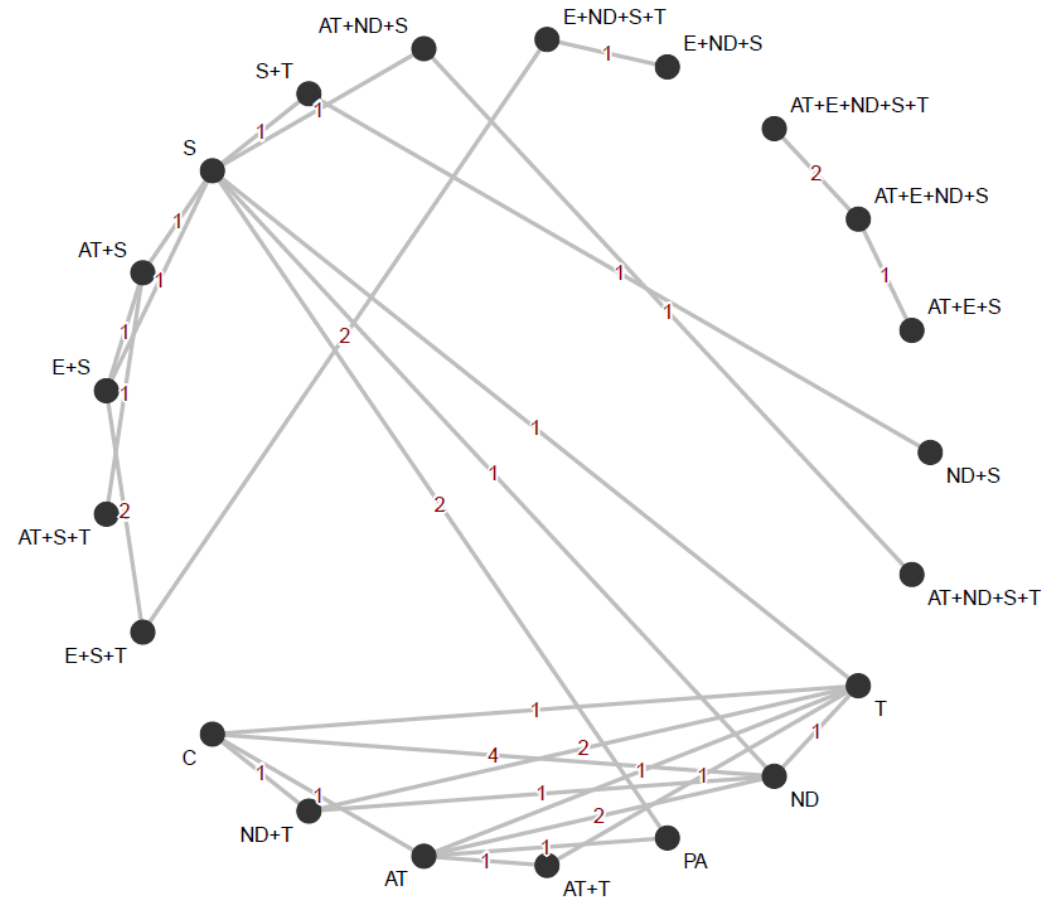
| | Q | d.f. | p-value |
|-----------------|-------|------|----------|
| Total | 98.18 | 12 | < 0.0001 |
| Within designs | 61.27 | 5 | < 0.0001 |
| Between designs | 28.83 | 7 | 0.0002 |

COMPONENT NETWORK META-ANÁLISIS (CNMA)

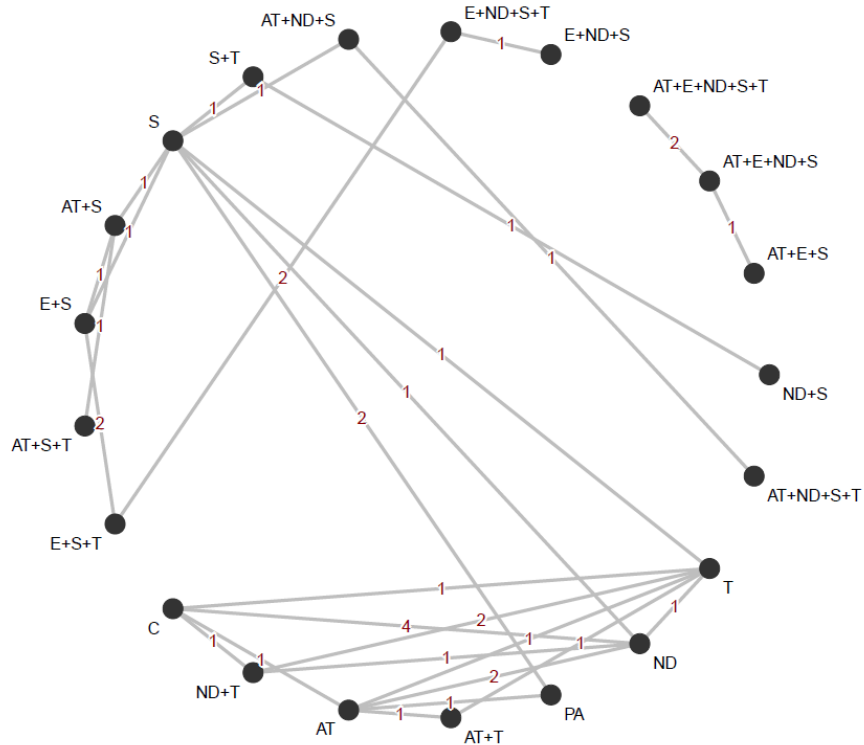
¿Qué es un CNMA?



¿Qué es un CNMA?



¿Qué es un CNMA?



| Intervention component (abbreviation) | Description |
|---------------------------------------|--|
| Articular treatment (AT) | Includes joint interventions focused on improving the movement of cervical, thoracic and glenohumeral structures (such as passive or active mobilization without resistance or manipulations) |
| Analgesic electrotherapy (E) | Electrotherapy interventions focused on reducing pain in the short term (such as TENS or interferential current) |
| Neurodynamic techniques (ND) | Intervention focused on mobilizing peripheral nerves or adopting joint positions that unload the nervous system to facilitate movement between the nervous system and its surrounding structures (interfaces) aimed at improving nerve function. |
| Physical activity counseling (PA) | Physical activity counseling consisting of global aerobic or muscular (non-specific) physical activity and being active. |
| Strength exercises (S) | Neck-specific strength training of deep cervical muscles. |
| Cervical Traction (T) | Included all types of cervical tractions. |

Resultados

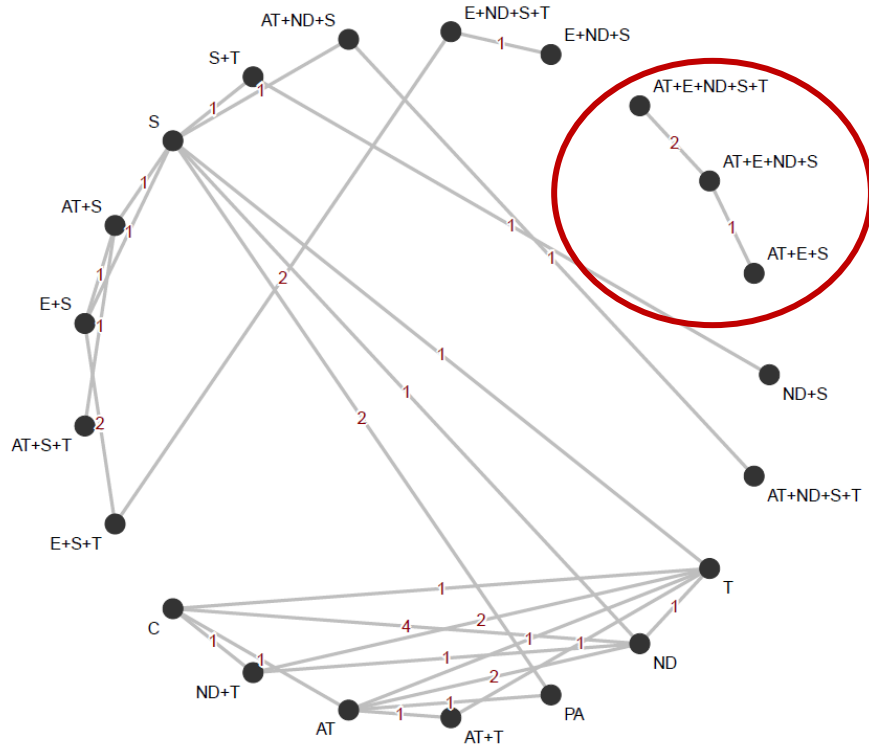


Table 2 Pooled SMD with 95% confidence interval (CI), 95% PrI and P-scores for NMA “A” and CNMA for each treatment versus control.

| Treatments | NMA estimates | | CNMA estimates | | P-Score (random) | |
|-------------|-----------------------------|-----------------------|-----------------------------|------|------------------|--|
| | SMD (95% CI) | 95% PrI | SMD (95% CI) | NMA | CNMA | |
| AT+E+ND+S+T | - | - | -3.24 [-5.92; -0.52] | - | 0.96 | |
| AT+ND+S+T | -0.73 [-3.78; 2.32] | [-4.69; 3.24] | -2.66 [-4.59; -0.73] | 0.34 | 0.88 | |
| E+ND+S+T | -4.75 [-7.82; -1.68] | [-8.73; -0.77] | -2.59 [-4.93; -0.25] | 0.95 | 0.85 | |
| AT+E+ND+S | - | - | -2.51 [-5.07; 0.05] | - | 0.82 | |
| ND+T | -1.97 [-3.33; -0.61] | [-4.47; 0.54] | -2.22 [-2.98; -1.46] | 0.61 | 0.80 | |
| AT+ND+S | -1.03 [-3.48; 1.42] | [-4.42; 2.36] | -1.94 [-3.70; -0.17] | 0.40 | 0.72 | |
| E+ND+S | -3.54 [-7.16; 0.09] | [-8.07; 0.99] | -1.86 [-4.07; 0.35] | 0.76 | 0.97 | |
| ND | -1.90 [-2.76; -1.03] | [-4.11; 0.32] | -1.49 [-2.01; -0.98] | 0.61 | 0.60 | |
| AT+T | -0.91 [-2.87; 1.05] | [-3.88; 2.06] | -1.37 [-2.33; -0.41] | 0.37 | 0.57 | |
| ND+S | -1.69 [-4.70; 1.32] | [-5.61; 2.23] | -1.29 [-2.71; 0.14] | 0.53 | 0.53 | |
| AT+S+T | -4.45 [-7.52; -1.38] | [-8.43; -0.47] | -1.17 [-2.93; 0.59] | 0.91 | 0.49 | |
| E+S+T | -3.66 [-6.41; -0.91] | [-7.33; 0.01] | -1.09 [-3.30; 1.11] | 0.83 | 0.45 | |
| AT+E+S | - | - | -1.02 [-3.45; 1.42] | - | 0.42 | |
| T | -0.94 [-2.13; 0.25] | [-3.34; 1.45] | -0.73 [-1.23; -0.22] | 0.38 | 0.35 | |
| AT | -0.69 [-1.90; 0.52] | [-3.10; 1.72] | -0.65 [-1.41; 0.12] | 0.32 | 0.32 | |
| S+T | -0.29 [-2.62; 2.04] | [-3.58; 2.99] | -0.52 [-1.94; 0.90] | 0.23 | 0.27 | |
| AT+S | -3.03 [-5.46; -0.60] | [-6.41; 0.35] | -0.44 [-2.03; 1.14] | 0.76 | 0.25 | |
| E+S | -1.79 [-4.19; 0.61] | [-5.14; 1.56] | -0.37 [-2.45; 1.72] | 0.54 | 0.23 | |
| PA | -0.03 [-1.67; 1.61] | [-2.74; 2.67] | 0.13 [-1.26; 1.51] | 0.16 | 0.12 | |
| S | -0.02 [-1.52; 1.48] | [-2.62; 2.58] | 0.21 [-1.03; 1.45] | 0.15 | 0.07 | |
| C | 0.00 [0.00; 0.00] | [0.00; 0.00] | 0.00 [0.00; 0.00] | 0.15 | 0.14 | |

Resultados

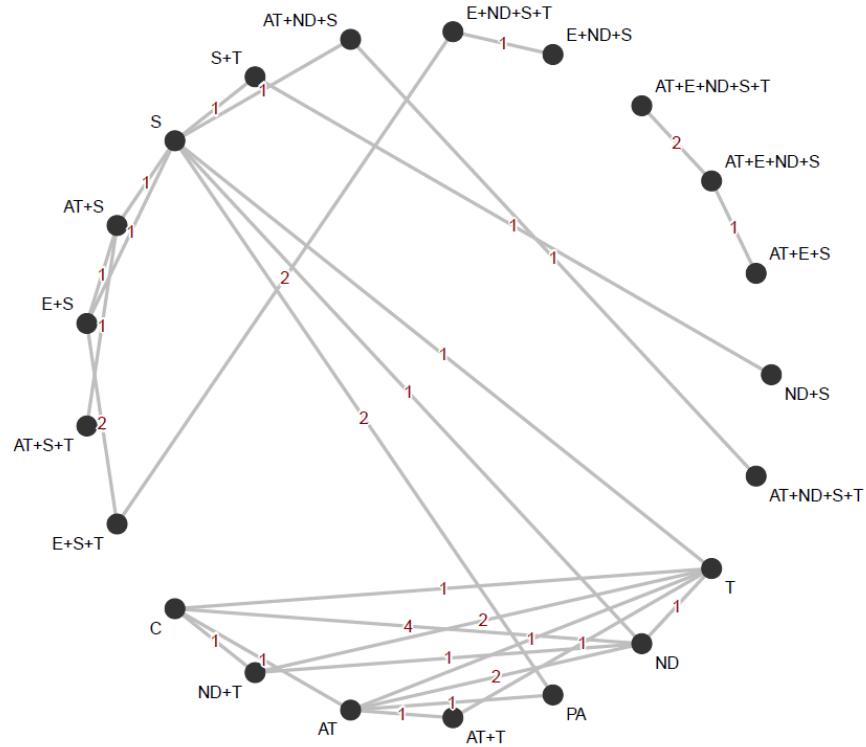


Table 1. Results for components (random effects models)

| Components | SMD (95% CI) | p value |
|------------|-----------------------------|--------------------|
| ND | -1.49 [-2.01; -0.98] | < 0.0001 |
| T | -0.73 [-1.23; -0.22] | 0.0046 |
| AT | -0.65 [-1.41; 0.12] | 0.0985 |
| E | -0.57 [-2.19; 1.04] | 0.4852 |
| PA | 0.13 [-1.26; 1.51] | 0.8576 |
| S | 0.21[-1.03; 1.45] | 0.7450 |

Resultados

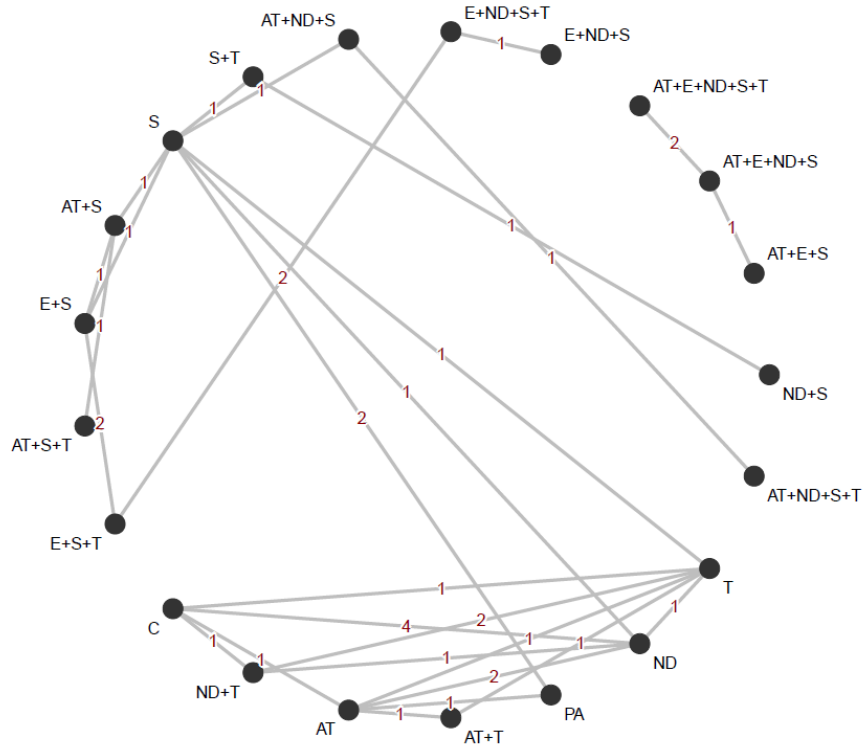


Table 1. Results for components (random effects models)

| Components | SMD (95% CI) | p value |
|------------|-----------------------------|--------------------|
| ND | -1.49 [-2.01; -0.98] | < 0.0001 |
| T | -0.73 [-1.23; -0.22] | 0.0046 |
| AT | -0.65 [-1.41; 0.12] | 0.0985 |
| E | -0.57 [-2.19; 1.04] | 0.4852 |
| PA | 0.13 [-1.26; 1.51] | 0.8576 |
| S | 0.21 [-1.03; 1.45] | 0.7450 |

Conclusiones

1. El NMA nos permite analizar todos los datos relacionados con una misma red utilizando evidencia directa e indirecta.
2. La evidencia del NMA es más conservadores y precisa que la de un MA convencional, siempre y cuando se cumplan los supuestos de consistencia y transitividad.
3. En redes con intervenciones complejas, puede ser interesante realizar un CNMA, para evitar resultados sesgados y tener en cuenta el valor de cada componente por separado

ANATOMÍA Y FISIOLOGÍA DEL NETWORK META-ANALYSIS

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