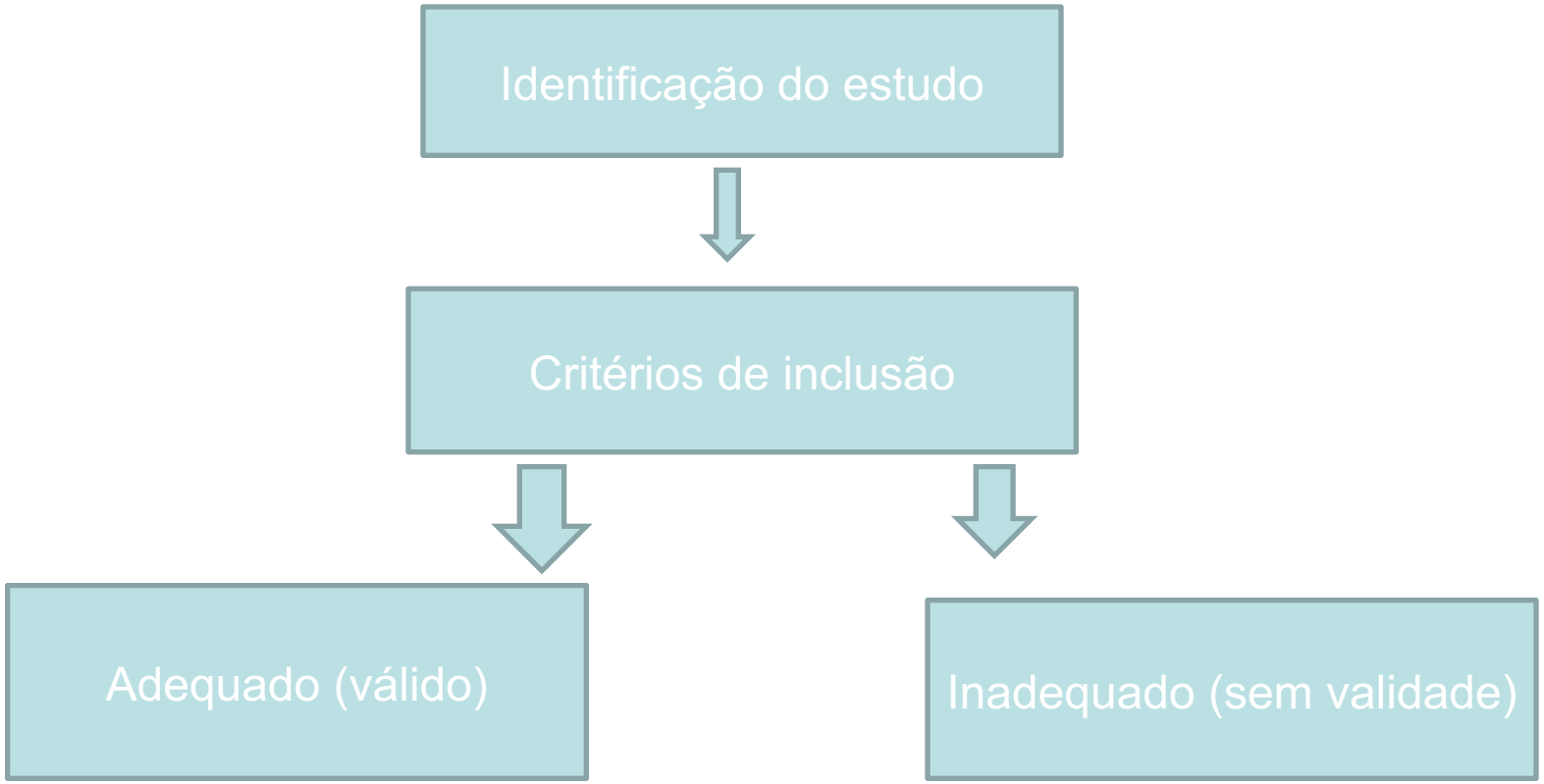
Avaliando a qualidade dos estudos

Suco de laranja

Inclusão de estudos

- Pode ser determinadas por características do delineamento que estão associadas a viés
  - Ensaio clínico:
    - Cegamento
    - Aleatorização
  - Estudos observacionais
    - Amamentação e performance em testes de inteligência
      - Estimativas ajustadas para ambiente doméstico (estimulação)


Identificação do estudo
Critérios de inclusão
Adequado (válido)
Inadequado (sem validade)

Estudo tem validade

- Preenche os critérios de inclusão
  - Relacionados ao delineamento
- Contribui para a meta-análise

Escalas para avaliar a qualidade dos estudos

Uso das escalas

- Critério de inclusão
  - Estudo precisa alcançar um certo escore
- Fonte de heterogeneidade
  - Estratifica a análise
- Fator de ponderação
  - Dando maior peso para os estudos com maior escore

Escalas mais comumente usadas

- Newcastle-Ottawa Scale (NOS)
  - Para estudos observacionais

Table 2: Quality assessment tools – comparison of key quality constructs

	Jadad	Sindhu	Downs & Black
Randomization	Max.= 2 points out of total score of 5 1. Was the study described as randomized? (1 point for yes) Give an additional point if the method to generate the sequence of randomization was described and it was appropriate. Deduct a point if it was inappropriate.	Max. = 10 points out of total score of 100 2. Have the patients been randomly allocated to treatment groups? (1 point for yes) If yes: i) Is the method of randomization explicitly detailed? (1.5 points) ii) Is it valid? i.e. Are there any threats to internal validity re: designation of subjects to groups? (2.5 points) iii) Is patient consent sought prior to randomization? (2.5 points) iv) Is it secure and 'blind' to the assessors? (2.5 points)	Max. = 2 points out of total score of 13 23. Were the study subjects randomised to intervention groups? Studies which state that subjects were randomised should be answered yes except where method of randomisation would not ensure random allocation. For example alternate allocation would score no... (1 point for yes) 24. Was the randomised intervention assignment concealed from both patients and health care staff until recruitment was complete and irrevocable? (1 point)
Blinding	Max. = 2 points out of total score of 5 2. Was the study described as double blind? (1 point) Give an additional point if the method of double blinding was described and it was appropriate. Deduct a point if it was inappropriate.	Max. = 5 points out of total score of 100 9. Is the assessment blind? a) If yes, who is blinded: i) patients? (2 points) ii) therapist/carer? (2 points) iii)assessor/data collector? (1 point) b) If no, i) are reasons given as to why assessment is not blind? (2 points) ii) Is there discussion of bias resulting from non-blind assessment? (3 points)	Max. = 2 points out of total score of 13 14. Was an attempt made to blind study subjects to the intervention they have received? (1 point) 15. Was an attempt made to blind those measuring the main outcomes of the intervention? (1 point)
Withdrawals and dropouts Intention to treat analysis	Max.= 1 point out of total score of 5 3. Was there a description of withdrawals and dropouts? 1 point)	Max. = 12 points out of total score of 100 6. Has an 'intention-to-treat analysis been performed? i.e. everyone randomized is retained in the study; everyone randomized is included in the final analysis; and no selective dropouts. (8 points) b) if not, is it clear what was done, its justification and impact on bias? (8 points) 11. Loss to follow-up a) (<) 20% loss to follow up (2 points) b) <10% loss to follow-up (2 points)	Max. = 2 points out of total score of 13 25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn? The questions should be answered no for trials if: the main conclusions of the study were based on analyses of treatment rather than intention to treat:... (1 point) 26. Were losses of patients to follow-up taken into account? If the number of patients lost to follow-up are not reported, the question should be answered unable to determine. If the proportion lost to follow-up was too small to affect the main findings, the question should be answered yes? (1 point)
Appropriate statistical analysis	no items	Max. = 6 points out of total score of 100 7. Statistical analysis a) Is the analysis appropriate/specific to the hypothesis and to the data? (1 point) b) Is the analysis adequately described? (1 point) c) Do the statistical assumptions hold? (1 point) d) Are adequate summary statistics provided at: i) baseline? (0.5 point) ii) outcome? (05. point) e) Is the overall significance level reported protected against inflation due to multiple testing? (1 point) f) If confounders exist, are they adjusted for via multivariate techniques even if differences between groups are not significant? (1 point)	Max. = 4 points out of total score of 13 16. If an of the results of the study were based in 'data dredging', was this made clear? (1 point) 17. Do the analyses adjust for different lengths of follow-up of patients? (1 point) 18. Were the statistical tests used to assess the main outcomes appropriate? (1 point) 25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn? (1 point)
Compliance with treatment	no items	Max. = 4 points out of total score of 100 14. Has patient compliance been assessed? (4 points)	Max. = 1 point out of total score of 13 19. Was compliance with the interventions reliable? (1 point)
Outcome Measures	no items	Max. = 14 points out of total score of 100 3. Measurement of outcomes a) Is the form of measurement stated? (3 points) b) Has an attempt been made to validate the measures? (3 points) c) Has an attempt been made to test the reliability of the measures? (2 points) d) Is the outcome objective as compared to subjective? (2 points) 12. Outcomes a) How many outcomes are used (1/2 point for each, to a max. of 2) b) Are they relevant? (1 point) c) Are they independent? (1 point)	Max. = 1 point out of total score of 13 20. Were the main outcome measures used accurate (valid and reliable)? (1 point)

Table 3: Systematic reviews of randomized oncology trials with sensitivity analysis exploring the relationship between study quality scores and effect sizes for mortality

Systematic Review	Interventions	Outcome	Quality Scale	Definition of High Quality	Effect Size (95% confidence interval)	
					All Studies (# studies)	High Quality (# studies)
McAlister et al, 1998 (26)	allogenic blood transfusion versus autologous or leucocyte-depleted allogenic blood during cancer surgery	relative risk of death*	Jadad (22)	score ≥3 out of 5	RR, 0.94 (0.76 to 1.16) (n = 5)	RR, 0.84 (0.47 to 1.52) (n = 2)
Caubet et al, 1997 (27)	nonsteroidal anti-androgens (plus LHRH or orchiectomy) versus LHRH or orchiectomy alone for advanced prostate cancer	relative risk of death*	Chalmers (31)	score ≥50 % of total possible score	RR, 0.81 (0.70 to 0.94) (n = 13)	RR, 0.78 (0.66 to 0.92) (n = 4)
Dube et al, 1997 (28)	adjuvant chemotherapy versus control for colorectal cancer	odds ratio for death*	Chalmers (31)	score >50 % of total possible score	OR, 0.82 (0.77 to 0.89) (n = 29)	OR, 0.77 (0.71 to 0.85) (n = 14)
Detsky et al, 1992 (29)	total parenteral nutrition versus control in cancer patients undergoing chemotherapy	odds ratio for survival**	Chalmers (31)	score >42 % of total possible score; quality score also used as a weighting factor in meta analysis	OR, 0.74 (0.42 to 1.3) (n = 8)	OR, 0.69 (0.38 to 1.3) (n = 2) weighted OR, 0.61 (0.23 to 1.6)
Klein et al, 1986 (30)	total parenteral nutrition versus control in cancer patients undergoing surgery	odds ratio for operative death*	Developed specifically for the systematic review	quality score used as a weighting factor in meta analysis	OR, 0.44 (0.21 to 0.90, p = 0.02) (n = 10)	weighted OR not reported but p = 0.07 after weighting for study quality

LHRH, luteinizing hormone-releasing hormone; RR, relative risk; OR, odds ratio
*RR or OR <1.0 indicates fewer deaths in the experimental group than in the control group
** OR <1.0 indicates more deaths in the experimental group than in the control group

Jadad

1. Was the study described as random? 1 0
2. Was the randomization scheme described and appropriate? 1 0
3. Was the study described as double-blind? 1 0
4. Was the method of double blinding appropriate? (Were both the patient and the assessor appropriately blinded?) 1 0
5. Was there a description of dropouts and withdrawals? 1 0

Downs & Black

- Reporting
  - *Is the hypothesis/aim/objective of the study clearly described?*
  - *Are the main outcomes to be measured clearly described in the Introduction or Methods section?*
  - *Are the characteristics of the patients included in the study clearly described ?*
  - *Are the interventions of interest clearly described?*
  - *Are the distributions of principal confounders in each group of subjects to be compared clearly described?*
  - *Are the main findings of the study clearly described?*
  - *Does the study provide estimates of the random variability in the data for the main outcomes?*
  - *Have all important adverse events that may be a consequence of the intervention been reported?*
  - *Have the characteristics of patients lost to follow-up been described?*
  - *Have actual probability values been reported(e.g. 0.035 rather than <0.05) for the main outcomes except where the probability*

External validity

- *Were the subjects asked to participate in the study representative of the entire population from which they were recruited?*
- *Were those subjects who were prepared to participate representative of the entire population from which they were recruited?*
- *Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?*

Internal validity

- *Was an attempt made to blind study subjects to the intervention they have received ?*
- *Was an attempt made to blind those measuring the main outcomes of the intervention?*
- *If any of the results of the study were based on "data dredging", was this made clear?*
- *In trials and cohort studies, do the analyses adjust for different lengths of follow-up of patients, or in case-control studies, is the time period between the intervention and outcome the same for cases and controls ?*
- *Were the statistical tests used to assess the main outcomes appropriate?*

Delineamento como fonte de heterogeneidade

O que este resultado sugere?

Table 3.2. Breastfeeding and the risk of overweight and obesity in later life: Random-effects meta-analyses of risk of overweight/obesity by subgroup

Subgroup analysis	Number of estimates	Pooled odds ratio and 95% confidence interval	P value
By age group			
1 to 9 years	22	0.79 (0.71 to 0.87)	0.001
9 to 19 years	11	0.69 (0.60 to 0.80)	0.001
>19 years	6	0.88 (0.74 to 1.04)	0.13
By study size			
<500 participants	11	0.51 (0.35 to 0.75)	0.001
500–1499 participants	11	0.79 (0.66 to 0.93)	0.006
≥1500 participants	17	0.80 (0.74 to 0.87)	0.001
By year at birth			
Before 1980	13	0.83 (0.73 to 0.95)	0.008
After 1980	22	0.78 (0.72 to 0.85)	0.001
By study design			
Cross-sectional	26	0.79 (0.72 to 0.87)	0.001
Case-control	3	0.58 (0.23 to 1.45)	0.24
Cohort	10	0.75 (0.69 to 0.83)	0.001
By length of recall of breastfeeding			
<3 years	24	0.79 (0.71 to 0.87)	0.001
≥3 years	15	0.76 (0.67 to 0.86)	0.001
By categorization of breastfeeding			
Ever breastfed	12	0.75 (0.67 to 0.83)	0.001
Breastfed for a given number of months	23	0.78 (0.71 to 0.86)	0.001
By control for confounding			
None	16	0.76 (0.64 to 0.91)	0.004
Adjusted for socioeconomic status	3	0.72 (0.66 to 0.79)	0.001
Adjusted for socioeconomic status and parental anthropometry	20	0.77 (0.71 to 0.84)	0.001
By study setting			
High-income country	33	0.77 (0.71 to 0.83)	0.001
Middle/Low-income country	6	0.82 (0.62 to 1.09)	0.18
Total	39	0.78 (0.72 to 0.84)	

Table 2.2. Breastfeeding and blood cholesterol in later life: Random-effects meta-analyses of cholesterol levels by subgroup

Subgroup analysis	Number of estimates of total cholesterol	Mean difference (95% confidence interval)	P value
By age group			
1 to 9 years	15	0.02 (-0.06 to 0.11)	0.63
9 to 19 years	4	-0.07 (-0.21 to 0.08)	0.37
>19 years	9	-0.18 (-0.30 to -0.06)	0.004
By study size			
<300 participants	20	-0.04 (-0.16 to 0.07)	0.47
≥300 participants	8	-0.01 (-0.08 to 0.06)	0.74
By year at birth			
Before 1980	17	-0.06 (-0.18 to 0.06)	0.32
After 1980	7	-0.02 (-0.10 to 0.06)	0.64
By study design			
Cross-sectional	18	-0.01 (-0.10 to 0.09)	0.88
Cohort	9	-0.05 (-0.14 to 0.05)	0.35
By length of recall of breastfeeding			
<3 years	21	0.00 (-0.07 to 0.08)	0.95
≥3 years	7	-0.13 (-0.27 to 0.01)	0.07
By categorization of breastfeeding			
Ever breastfed	17	-0.07 (-0.16 to 0.01)	0.08
Breastfed for a given number of months	11	0.01 (-0.11 to 0.13)	0.82
By control for confounding			
None	23	-0.04 (-0.14 to 0.06)	0.45
Adjusted for socioeconomic and demographic variables	5	-0.02 (-0.09 to 0.05)	0.55
By control for current measure of body size			
No	24	-0.01 (-0.07 to 0.06)	0.91
Yes	4	-0.20 (-0.33 to -0.06)	0.006
Total	28	-0.03 (-0.10 to 0.03)	

TABLE 1—Odds Ratios for Weaning by 3 Months, According to Study Quality Items: Meta-Analysis of 13 Studies, 1979–1997

	Odds Ratio	95% Confidence Interval
Interviewer unaware of research hypothesis or exposure status		
Yes	1.63	1.00, 2.67
No	2.02	1.16, 3.50
Maternal smoking		
Yes	1.88	1.35, 2.62
No	1.99	1.26, 3.14
Losses to follow-up, %		
<15 and symmetrical for both groups	1.60	1.26, 2.01
15–25 and symmetrical for both groups	3.71	2.09, 6.56
>25 or asymmetrical	1.94	1.35, 2.79
Recall for exposure and outcome data		
≤6 months	2.13	1.60, 2.83
>6 months for either exposure or outcome	1.68	0.98, 2.87
>6 months for both exposure and outcome	1.58	0.78, 3.22
Adjustment for covariates		
Full adjustment	1.71	1.34, 2.18
Partial adjustment	2.47	1.43, 4.27
No adjustment	2.82	1.40, 5.68

TABLE 2. Association Between Methodological Covariates and Geographic Area With ADHD/HD Prevalence Estimates

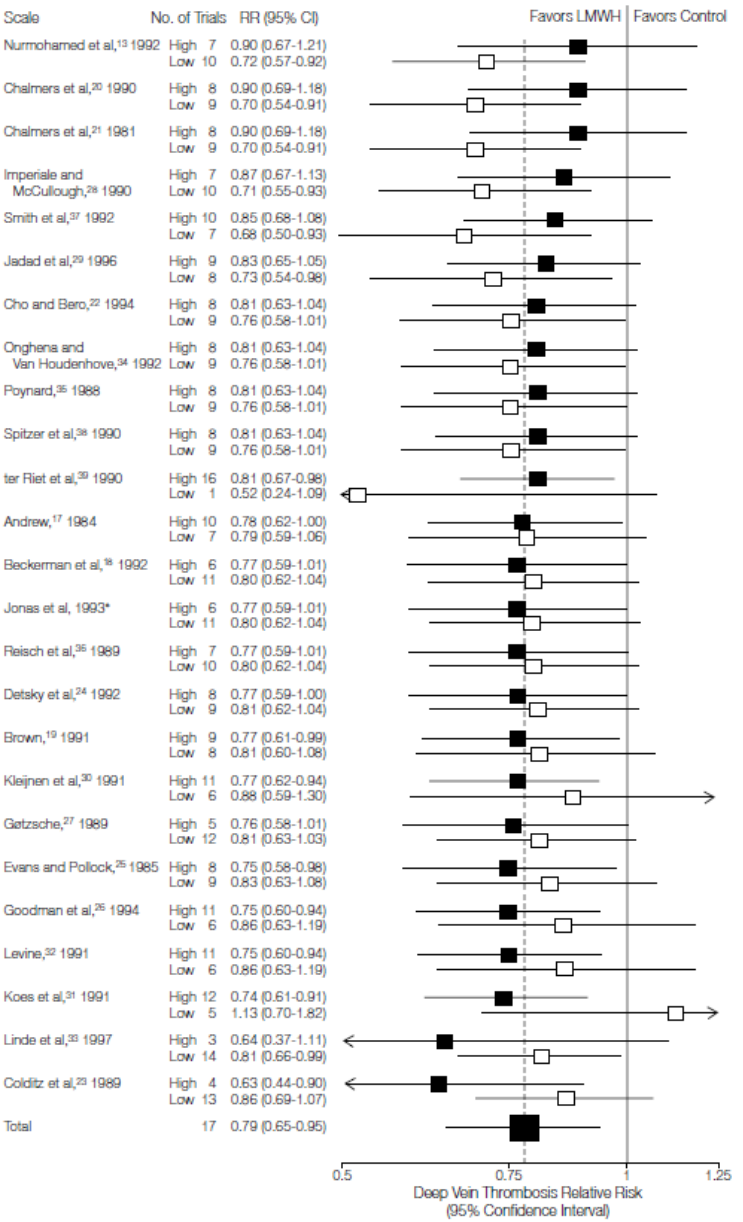
Variable	Univariate Model p	Metaregression (Multivariate Model)[a] p
Origin of sample	<0.001	
Community		index
School		0.38
Source of information	<0.001	
Best-estimate procedure		index
"And rule"		0.04
Parents		0.03
"Or rule"		0.003
Teachers		<0.001
Subjects		0.46
Impairment criterion	<0.001	
Yes		index
No		0.001
Diagnostic criteria	<0.001	
DSM-IV		index
DSM-III-R		0.02
DSM-III		0.69
ICD-10		0.005
Number of stages of evaluation	<0.001	
One		index
Two		0.25
Two, only screens positive at first stage[b]		0.31
Response rate	0.25	—
Sample size	<0.001	0.81
Geographic area	0.009	
North America		index
Europe		0.40
Oceania		0.45
South America		0.83
Asia		0.85
Africa		0.03
Middle East		0.01

[a] Between-study variance assessed by moment-based estimate (tau 2=7.815).

[b] Studies using two-stage sampling where only screening positives were assessed in the second stage (for details see the data supplement of the online version of this article).

Comparando a performance de diferentes escalas

Figure 1. Results From Sensitivity Analyses Dividing Trials in High- and Low-Quality Strata, Using 25 Different Quality Assessment Scales



Relative risks (RRs) for deep vein thrombosis with 95% confidence intervals (CIs) are shown. LMWH indicates low-molecular-weight heparin. Black squares indicate estimates from high-quality trials and open squares indicate estimates from low-quality trials. Arrows indicate that the values are outside the range of the x axis. Broken line indicates combined estimate from all 17 trials. Solid line indicates null effect line. The scales are arranged in decreasing order of the RRs in trials deemed to be of high quality. Asterisk indicates unpublished scale.

O que aconteceu ?

- Escalas medem
  - Delineamento
  - Redação

O que aconteceu ?

- O mesmo peso para cada ítem
  - Item 1 – Downs & Black
    - Hipótese e objetivos claramente descritos
  - Item 14 – Downs & Black
    - Os indivíduos estavam cegos da intervenção

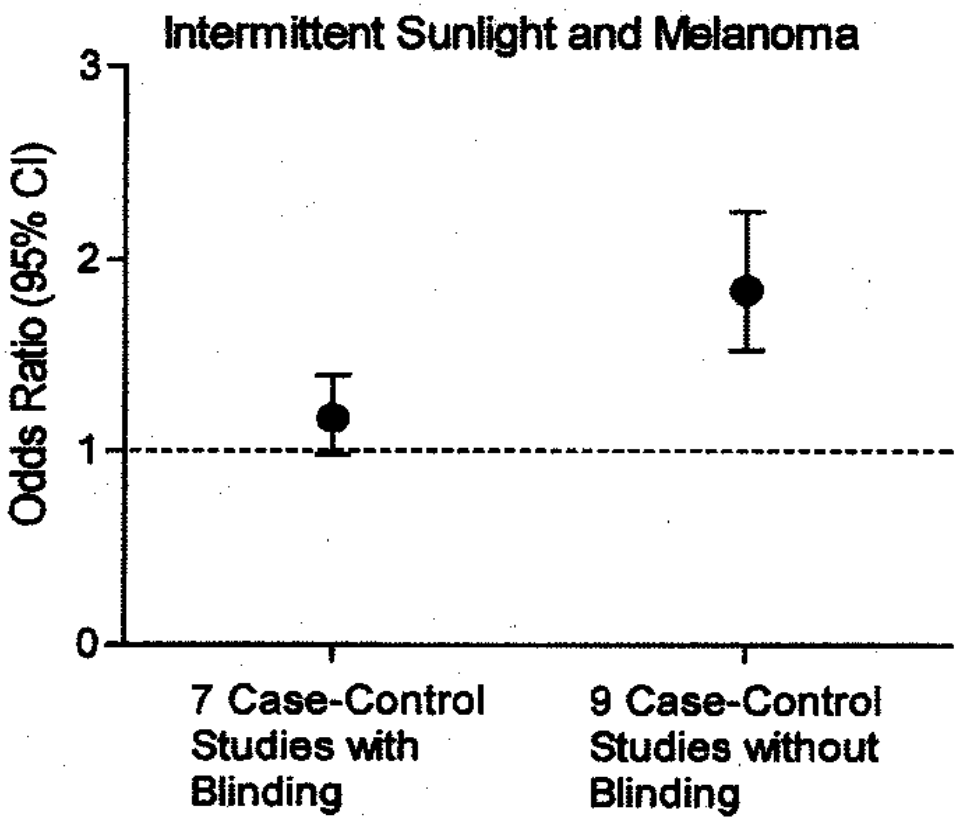
- Nem todos os aspectos relacionados ao delineamento tem a mesma influência

Juni et al – JAMA 1999

Table 3. Results From Univariate Meta-Regression Analysis Relating Methodological Key Domains to Effect Sizes in 17 Trials Comparing Heparins for Thromboprophylaxis in General Surgery*

Methodological Domain	No. of Trials	Ratio of Relative Risks (95% CI)	*P* Value
Concealment of randomization			
Yes	6	1.00 (Referent)	.58
Unclear	11	1.12 (0.76-1.65)	
Blinding of outcome assessments			
Yes	11	1.00 (Referent)	.046
No	6	0.65 (0.43-0.99)	
Handling of dropouts and withdrawals			
Intention-to-treat analysis performed	7	1.00 (Referent)	.12
Intention-to-treat analysis not performed	10	1.37 (0.92-2.03)	

*CI indicates confidence interval. A ratio of relative risks of less than 1 indicates that methodologically inferior trials exaggerate the benefits of low-molecular-weight heparins compared with the referent group. A ratio of relative risks above 1 indicates the opposite.


Intermittent Sunlight and Melanoma
Odds Ratio (95% CI)
3
2
1
0
7 Case-Control Studies with Blinding
9 Case-Control Studies without Blinding

Além disso

- Se o estudo tem viés, que invalida as evidências
  - Do que adianta o restante
    - Deve ser excluído

O que fazer

- Avaliar separadamente diferentes aspectos relacionados ao delineamento
- Estratificar a análise
  - Identificar fontes de heterogeneidade
- Usar meta-regressão
  - Para avaliar contribuição de diferentes fontes de heterogeneidade

Suco de laranja

Revisão Sistemática e Meta-Análise

Meta-Regressão

Efeitos randômicos

- Incorpora a heterogeneidade na estimativa do pooled effect
  - Mas não explica a heterogeneidade

- Devemos sempre tentar explicar a heterogeneidade

- Estratificação
  - Mostra se existe ou não modificação de efeito
- Não responde qual é a contribuição de cada covariável para o total da heterogeneidade

TABLE 1—Odds Ratios for Weaning by 3 Months, According to Study Quality Items: Meta-Analysis of 13 Studies, 1979–1997

	Odds Ratio	95% Confidence Interval
Interviewer unaware of research hypothesis or exposure status		
Yes	1.63	1.00, 2.67
No	2.02	1.16, 3.50
Maternal smoking		
Yes	1.88	1.35, 2.62
No	1.99	1.26, 3.14
Losses to follow-up, %		
<15 and symmetrical for both groups	1.60	1.26, 2.01
15–25 and symmetrical for both groups	3.71	2.09, 6.56
>25 or asymmetrical	1.94	1.35, 2.79
Recall for exposure and outcome data		
≤6 months	2.13	1.60, 2.83
>6 months for either exposure or outcome	1.68	0.98, 2.87
>6 months for both exposure and outcome	1.58	0.78, 3.22
Adjustment for covariates		
Full adjustment	1.71	1.34, 2.18
Partial adjustment	2.47	1.43, 4.27
No adjustment	2.82	1.40, 5.68

Meta-regressão

- Permite a avaliação da contribuição de cada covariável para a explicação da heterogeneidade
- O peso de cada estudo incorpora a variância dentro dos estudos ($SE(\theta_i)^2$) e entre estudos τ^2 (como no modelo randômico):

$$w'_i = \frac{1}{SE(\theta_i)^2 + \tau^2}$$

Meta-Regressão

- t^2 irá levar as covariáveis em consideração
- Produzindo pesos que refletem as diferentes fontes de heterogeneidade destas variáveis

- Uma vez que τ^2 foi estimado e os pesos calculados w'_i, é rodado um modelo de regressão ponderado, tendo ln(OR) como desfecho e as características dos estudos como preditores (covariáveis)

$$y_i = \alpha + \beta\, x_i$$

- Se a covariável não é uma fonte de heterogeneidade, ela não estará associada com o desfecho, e β não será estatisticamente significativo.

- No modelo sem covariáveis, a equação é reduzida para $y_i = \alpha$
- α representa o pooled effect do ln(OR)
- Ou seja, o resultado deverá ser igual ao do modelo com efeitos randômicos.

Estimativa com efeitos aleatórios

$$\theta_{DL} = \frac{\sum_i w'_i \, \theta_i}{\sum_i w'_i}$$

Peso incorpora a heterogeneidade:

$$w'_i = \frac{1}{SE(\theta_i)^2 + \tau^2}$$

Comando no STATA

- Metareg logor covariates, wsse(selogor)
- Covariates – fontes de heterogeneidade
- LOGOR e SELOGOR – transformados em logaritmo natural

```
. metareg meansys, wsse(sesys) mm

Meta-regression                                           Number of obs  =      30
Method of moments estimate of between-study variance      tau2           =   .7798
% residual variation due to heterogeneity                 I-squared_res  =  53.69%
With Knapp-Hartung modification
```

meansys	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
_cons	-1.211408	.277732	-4.36	0.000	-1.779433	-.6433819

```
. meta meansys sesys

Meta-analysis

       |  Pooled      95% CI          Asymptotic      No. of
Method |     Est   Lower   Upper  z_value  p_value   studies
-------+-----------------------------------------------------
Fixed  |  -0.830  -1.112  -0.547   -5.750    0.000      30
Random |  -1.211  -1.721  -0.702   -4.663    0.000

Test for heterogeneity: Q= 62.618 on 29 degrees of freedom (p= 0.000)
Moment-based estimate of between studies variance =  0.780
```

```
. meta meansys sesys

Meta-analysis

       |  Pooled      95% CI         Asymptotic      No. of
Method |     Est   Lower   Upper  z_value  p_value   studies
-------+-----------------------------------------------------
Fixed  |  -0.830  -1.112  -0.547   -5.750    0.000     30
Random |  -1.211  -1.721  -0.702   -4.663    0.000

Test for heterogeneity: Q= 62.618 on 29 degrees of freedom (p= 0.000)
Moment-based estimate of between studies variance =  0.780

. metareg meansys, wsse(sesys)

Meta-regression                                         Number of obs  =      30
REML estimate of between-study variance                 tau2           =   1.174
% residual variation due to heterogeneity               I-squared_res  =  53.69%
With Knapp-Hartung modification
------------------------------------------------------------------------------
     meansys |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       _cons |  -1.277657   .2913937    -4.38   0.000    -1.873625   -.6816904
------------------------------------------------------------------------------

. metareg meansys, wsse(sesys) mm

Meta-regression                                         Number of obs  =      30
Method of moments estimate of between-study variance    tau2           =   .7798
% residual variation due to heterogeneity               I-squared_res  =  53.69%
With Knapp-Hartung modification
------------------------------------------------------------------------------
     meansys |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       _cons |  -1.211408    .277732    -4.36   0.000    -1.779433   -.6433819
------------------------------------------------------------------------------
```

metareg theta tool, wsse(setheta) bs(mm)

```
Meta-analysis regression                    No of studies =   6
                                            tau^2 method      mm
                                            tau^2 estimate =  .0927

------------------------------------------------------------------------------
      |    Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
------+-----------------------------------------------------------------------
 tool |  -.22139   .34703    -0.64   0.524     -.90156    .45878
_cons |  -.06518   .50061    -0.13   0.896     -1.0463    .91599
------------------------------------------------------------------------------
```

metareg theta study_type, wsse(setheta) bs(mm)

```
Meta-analysis regression                    No of studies =   6
                                            tau^2 method      mm
                                            tau^2 estimate =  0

------------------------------------------------------------------------------
           |    Coef.  Std. Err.      z    P>|z|     [95% ConfInterval]
-----------+------------------------------------------------------------------
study_type |   .34840   .12123     2.87   0.004      .11079    .58601
     _cons |  -.83009   .20933    -3.97   0.000     -1.2403   -.41980
------------------------------------------------------------------------------
```

```
. meta logrr selogrr

Meta-analysis

       |  Pooled      95% CI          Asymptotic      No. of
Method |     Est   Lower   Upper  z_value  p_value   studies
-------+-----------------------------------------------------
Fixed  |  -0.314  -0.405  -0.223   -6.755    0.000        11
Random |  -0.677  -1.090  -0.264   -3.213    0.001

Test for heterogeneity: Q= 125.626 on 10 degrees of freedom (p= 0.000)
Moment-based estimate of between studies variance =  0.382

. metareg logrr, wsse(selogrr)

Meta-regression                                 Number of obs  =        11
REML estimate of between-study variance         tau2           =    .3703
% residual variation due to heterogeneity       I-squared_res  =   92.04%
With Knapp-Hartung modification
```

logrr	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
_cons	-.6766679	.2098213	-3.22	0.009	-1.144179	-.2091568

Qual é o percentual da heterogeneidade que é explicad ude

Indica o percentual da variância residual que é atribuível a heterogeneidade entre os estudos

```
. metareg logrr  latitude, wsse(selogrr)

Meta-regression                                 mber of obs  =        11
REML estimate of between-study variance         au2          =        .1
% residual variation due to heterogeneity       I-squared_res =   61.80%
Proportion of between-study variance explained  Adj R-squared =   72.99%
With Knapp-Hartung modification
```

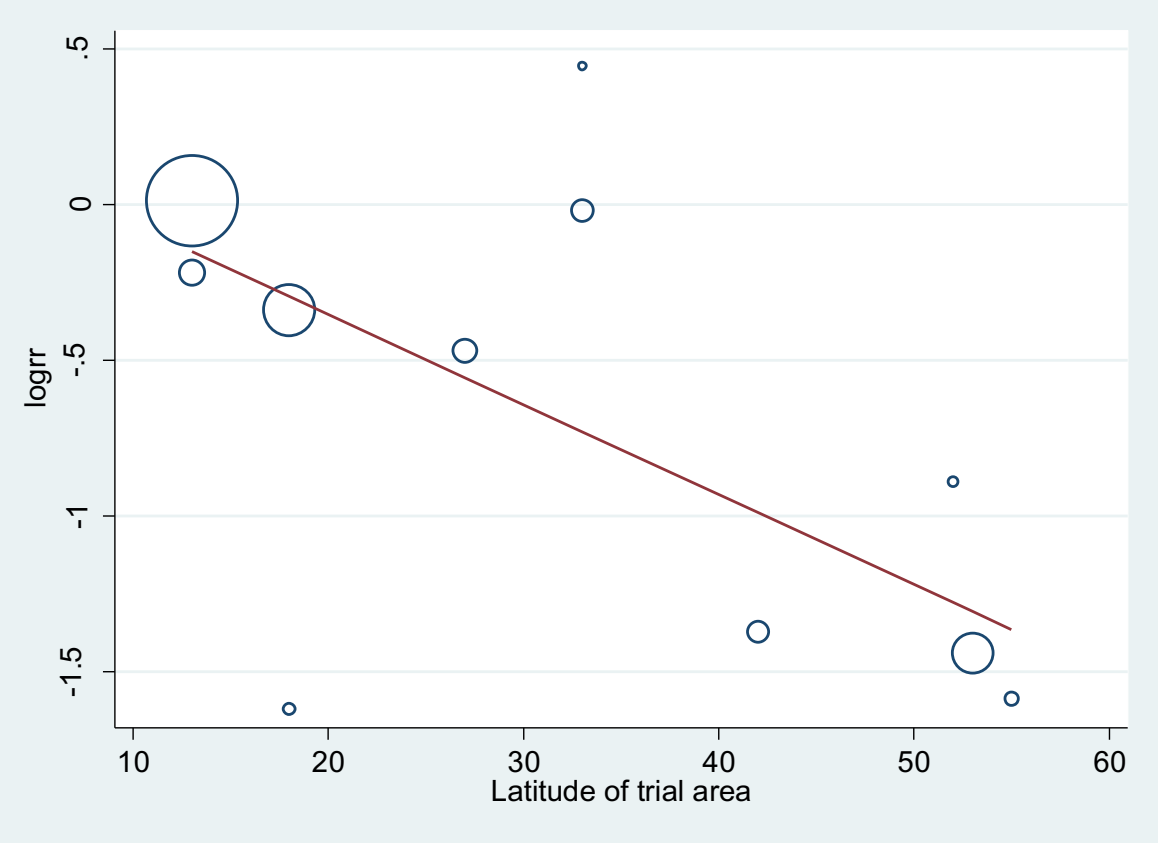
logrr	Coef.	St	[95% Conf.	Interval]
latitude	-.0288849	.0	-.050576	-.0071938
_cons	.2247162	.3	-.5026402	.9520726

Indica o percentual da heterogeneidade que é explicado pelas covariáveis

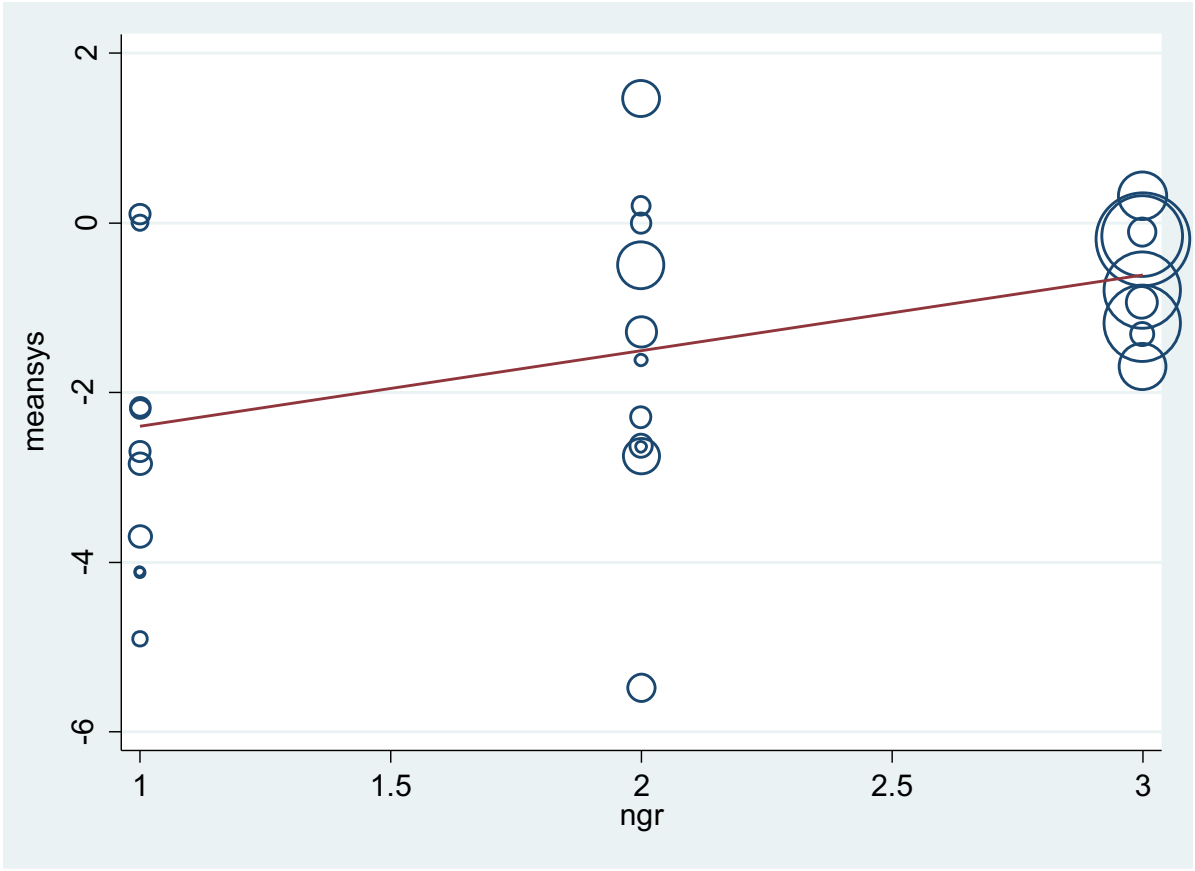
```
. metareg Mean, wsse(SD) bs(mm)

Meta-analysis regression                        No of studies =   28
                                          tau^2 method      mm
                                          tau^2 estimate =  .0085

------------------------------------------------------------------------------
             |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       _cons |  -.0322778   .0326626    -0.99   0.323    -.0962954    .0317397
------------------------------------------------------------------------------

. xi:metareg Mean i.age3gr, wsse(SD) bs(mm)
i.age3gr          _lage3gr_1-3        (naturally coded; _lage3gr_1 omitted)

Meta-analysis regression                        No of studies =   28
                                          tau^2 method      mm
                                          tau^2 estimate =  .0075

------------------------------------------------------------------------------
             |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
  _lage3gr_2 |  -.0930398   .0888444    -1.05   0.295    -.2671716     .081092
  _lage3gr_3 |  -.2036708    .083708    -2.43   0.015    -.3677355   -.0396062
       _cons |    .021161   .0390722     0.54   0.588    -.0554191    .0977411
------------------------------------------------------------------------------
```

- Qual é o efeito da amamentação sobre o nível de colesterol total, nos adultos
- 0.021161 -0.2036708

metareg logrr latitude, wsse(selogrr) graph



```
. metareg meansys ngr, wsse(sesys) graph

Meta-regression                                         Number of obs  =      30
REML estimate of between-study variance                 tau2           =   .7926
% residual variation due to heterogeneity               I-squared_res  =  43.91%
Proportion of between-study variance explained          Adj R-squared  =  32.49%
With Knapp-Hartung modification
------------------------------------------------------------------------------
     meansys |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         ngr |   .8894821   .3452739     2.58   0.016     .1822207    1.596744
       _cons |  -3.284084   .8448453    -3.89   0.001    -5.014671   -1.553497
------------------------------------------------------------------------------
```


meansys
2
0
-2
-4
-6
1
1.5
2
2.5
3
ngr

Article

The Worldwide Prevalence of ADHD: A Systematic Review and Metaregression Analysis

Guilherme Polanczyk, M.D.

Maurício Silva de Lima, M.D., Ph.D.

Bernardo Lessa Horta, M.D., Ph.D.

Joseph Biederman, M.D.

Luis Augusto Rohde, M.D., Ph.D.

Objective: The worldwide prevalence estimates of attention deficit hyperactivity disorder (ADHD)/hyperkinetic disorder (HD) are highly heterogeneous. Presently, the reasons for this discrepancy remain poorly understood. The purpose of this study was to determine the possible causes of the varied worldwide estimates of the disorder and to compute its worldwide pooled prevalence.

Method: The authors searched MEDLINE and PsycINFO databases from January 1978 to December 2005 and reviewed textbooks and reference lists of the studies selected. Authors of relevant articles from North America, South America, Europe, Africa, Asia, Oceania, and the Middle East and ADHD/HD experts were contacted. Surveys were included if they reported point prevalence of ADHD/HD for subjects 18 years of age or younger from the general population or schools according to DSM or ICD criteria.

Results: The literature search generated 9,105 records, and 303 full-text articles were reviewed. One hundred and two studies comprising 171,756 subjects from all world regions were included. The ADHD/HD worldwide-pooled prevalence was 5.29%. This estimate was associated with significant variability. In the multivariate metaregression model, diagnostic criteria, source of information, requirement of impairment for diagnosis, and geographic origin of the studies were significantly associated with ADHD/HD prevalence rates. Geographic location was associated with significant variability only between estimates from North America and both Africa and the Middle East. No significant differences were found between Europe and North America.

Conclusions: Our findings suggest that geographic location plays a limited role in the reasons for the large variability of ADHD/HD prevalence estimates worldwide. Instead, this variability seems to be explained primarily by the methodological characteristics of studies.

(Am J Psychiatry 2007; 164:942–948)

FIGURE 2. ADHD/HD Pooled Prevalence According to Demographic Characteristics and Geographic Location

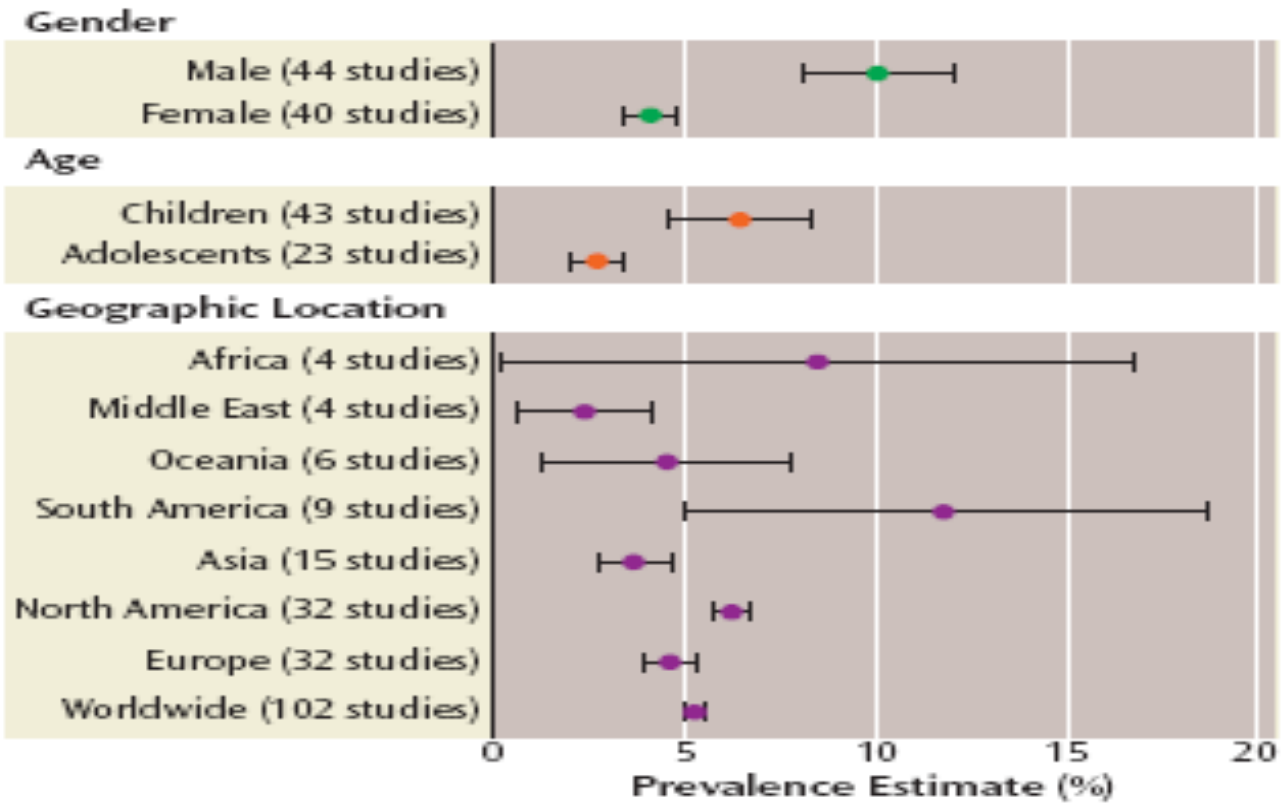


TABLE 2. Association Between Methodological Covariates and Geographic Area With ADHD/HD Prevalence Estimates

Variable	Univariate Model p	Metaregression (Multivariate Model)[a] p
Origin of sample	<0.001	
Community		index
School		0.38
Source of information	<0.001	
Best-estimate procedure		index
"And rule"		0.04
Parents		0.03
"Or rule"		0.003
Teachers		<0.001
Subjects		0.46
Impairment criterion	<0.001	
Yes		index
No		0.001
Diagnostic criteria	<0.001	
DSM-IV		index
DSM-III-R		0.02
DSM-III		0.69
ICD-10		0.005
Number of stages of evaluation	<0.001	
One		index
Two		0.25
Two, only screens positive at first stage[b]		0.31
Response rate	0.25	—
Sample size	<0.001	0.81
Geographic area	0.009	
North America		index
Europe		0.40
Oceania		0.45
South America		0.83
Asia		0.85
Africa		0.03
Middle East		0.01

[a] Between-study variance assessed by moment-based estimate (tau, 2=7.815).

[b] Studies using two-stage sampling where only screening positives were assessed in second state (for details see the data supplement of the online version of this article).