Fake Anabolic Androgenic Steroids on the Black Market – a systematic review and meta-analysis

MAIN OUTCOME 1: Proportions of counterfeit AAS-samples

Proportions of counterfeit anabolic androgenic steroids from 18 studies, grouped by geographical region

Study	Events	Total		Proportion	95%-CI
Region = Europe Weber C., et. al., 2017, Switzerland Fabresse N., et.al., 2021, France Odoardi A., et. al., 2021, Italy Krug O., et. al., 2014, Germany Graham M., et. al., 2009, United Kingdom Tircova B., et. al., 2019, Czech Republic/ Slovakia Thevis M. et. al., 2008, Germany Coopman V., et. al., 2012, Belgium Pellegrini M., et. al., 2011, Belgium Forsdahl, G. et. al., 2011, Austria Random effects model Prediction interval Heterogeneity: $l^2 = 95\%$, $\tau^2 = 0.3913$, $p < 0.01$	528 22 192 17 73 16 22 10 15 1 8	889 54 267 337 42 358 50 56 15 37 9 28 2142	***	0.59 0.41 0.19 0.57 0.40 0.20 0.32 0.39 - 0.67 0.41 0.11 0.29 0.37	$\begin{matrix} [0.56; 0.63]\\ [0.28; 0.55]\\ [0.15; 0.25]\\ [0.51; 0.62]\\ [0.26; 0.57]\\ [0.26; 0.57]\\ [0.20; 0.47]\\ [0.20; 0.47]\\ [0.26; 0.53]\\ [0.38; 0.88]\\ [0.25; 0.58]\\ [0.00; 0.48]\\ [0.13; 0.49]\\ [0.28; 0.48]\\ [0.12; 0.72] \end{matrix}$
Region = Brazil Neves D., et. al. 2013, Brazil Neves D., et. al. 2017, Brazil Ribeiro M., et. al., 2018, Brazil Berneira L., et. al., 2019, Brazil Riberio M., et. al., 2018, Brazil Lemos, V. F. et. al., 2021, Brazil Random effects model Prediction interval Heterogeneity: $I^2 = 54\%$, $\tau^2 = 0$, $p = 0.05$ Random effects model Prediction interval	1167 138 8 2 4 9	2818 328 40 8 16 30 3240 5382		0.41 0.42 0.20 0.25 0.25 0.30 0.41 0.36	[0.40; 0.43] [0.37; 0.48] [0.09; 0.36] [0.03; 0.65] [0.07; 0.52] [0.15; 0.49] [0.39; 0.43] [0.39; 0.43] [0.29; 0.43] [0.29; 0.43]
Heterogeneity: $l^2 = 94\%$, $\tau^2 = 0.3108$, $p < 0.01$ Test for subgroup differences: $\chi_1^2 = 0.53$, df = 1 ($p = 0$.47)		0.2 0.4 0.6 0.8		,

Number of studies combined: k = 18 Number of observations: o = 5382 Number of events: e = 2284

proportion	95%-CI
Random effects model	0.3573 [0.2869; 0.4346]
Prediction interval	[0.1403; 0.6545]

Quantifying heterogeneity:

tau² = 0.3108; tau = 0.5575; l² = 93.7% [91.4%; 95.4%]; H = 3.98 [3.41; 4.65]

Test of heterogeneity:

Q d.f. p-value Test 269.34 17 < 0.0001 Wald-type 301.17 17 < 0.0001 Likelihood-Ratio

Results for subgroups (random effects model):

k proportion 95%-Cl tau^2 tau Q l^2 Region = Europe 12 0.3742 [0.2770; 0.4828] 0.3913 0.6256 244.19 95.5% Region = Brazil 6 0.4099 [0.3879; 0.4323] 0 0 10.94 54.3%

Test for subgroup differences (random effects model):

Q d.f. p-value Between groups 0.53 1 0.4662

Prediction intervals for subgroups:

95%-PI

Region = Europe [0.1214; 0.7213] Region = Brazil [0.3861; 0.4341]

Details on meta-analytical method:

- Random intercept logistic regression model

- Maximum-likelihood estimator for tau^2

- Hartung-Knapp adjustment for random effects model

- Logit transformation

- Clopper-Pearson confidence interval for individual studies





Review: Counterfeit

Linear regression test of funnel plot asymmetry Test result: t = -0.80, df = 16, p-value = 0.4365

Sample estimates:

bias se.bias intercept se.intercept

-10.3550 12.9735 -0.2476 0.1206

Details:

- multiplicative residual heterogeneity variance (tau² = 16.1889)
- predictor: inverse of total sample size
- weight: inverse variance of average event probability
- reference: Peters et al. (2006), JAMA

Meta-regression by publication year



Meta-regression of counterfeit anabolic androgenic steroids from 18 studies by publication year

Mixed-Effects Model (k = 18; tau² estimator: ML)

tau^2 (estimated amount of residual heterogeneity): 0.2842
tau (square root of estimated tau^2 value): 0.5331
I^2 (residual heterogeneity / unaccounted variability): 92.2615%
H^2 (unaccounted variability / sampling variability): 12.9224

Tests for Residual Heterogeneity:

Wld(df = 16) = 265.3596, p-val < .0001 LRT(df = 16) = 289.6485, p-val < .0001

Test of Moderators (coefficient 2):

F(df1 = 1, df2 = 16) = 1.5458, p-val = 0.2317

Model Results:

estimate se tval df pval ci.lb ci.ub intrcpt 62.8358 51.0089 1.2319 16 0.2358 -45.2983 170.9699 Publ.Year -0.0315 0.0253 -1.2433 16 0.2317 -0.0852 0.0222

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

MAIN OUTCOME 2: Proportions of substandard AAS-samples

Proportions of substandard anabolic androgenic steroids from 8 studies, grouped by geographical region

Study	Events	Total		Proportion	95%-CI
Region = Europe Weber C., et. al., 2017, Switzerland Fabresse N., et.al., 2021, France Tircova B., et. al., 2019, Czech Republic/ Slovakia Pellegrini M., et. al., 2012, Italy Kozlik, P. et al., 2016, Slovakia Random effects model Prediction interval Heterogeneity: $I^2 = 95\%$, $\tau^2 = 0.2853$, $p < 0.01$	383 20 73 3 2	779 54 358 15 9 1215	* * * *	0.49 0.37 0.20 0.20 0.22 0.31	[0.46; 0.53] [0.24; 0.51] [0.16; 0.25] [0.04; 0.48] [0.03; 0.60] [0.17; 0.50] [0.06; 0.76]
Region = Brazil Neves D., et. al. 2017, Brazil Ribeiro M., et. al., 2018, Brazil Campos E., et. al., 2020, Brazil Random effects model Prediction interval Heterogeneity: $I^2 = 97\%$, $\tau^2 = 3.1195$, $p < 0.01$	36 23 28	328 40 31 399 -	*	0.11 0.58 0.90 0.53	[0.08; 0.15] [0.41; 0.73] [0.74; 0.98] [0.01; 0.99] [0.00; 1.00]
Random effects model Prediction interval Heterogeneity: $I^2 = 96\%$, $\tau^2 = 1.4382$, $p < 0.01$ Test for subgroup differences: $\chi^2_1 = 0.71$, df = 1 ($p = 0$.40)	1614	0.2 0.4 0.6 0.8	0.37	[0.17; 0.63] [0.02; 0.93]

Number of studies combined: k = 8Number of observations: o = 1614

Number of events: e = 568

proportion	95%-CI
Random effects model	0.3683 [0.1681; 0.6273]
Prediction interval	[0.0248; 0.9304]

Quantifying heterogeneity:

tau² = 1.4382; tau = 1.1993; l² = 96.4% [94.7%; 97.6%]; H = 5.29 [4.33; 6.48]

Test of heterogeneity:

Q d.f. p-value Test 196.24 7 < 0.0001 Wald-type 254.95 7 < 0.0001 Likelihood-Ratio

Results for subgroups (random effects model):

95%-Cl tau^2 tau Q I^2 k proportion Region = Europe 5 0.3096 [0.1664; 0.5017] 0.2853 0.5341 83.25 95.2% Region = Brazil 3 0.5289 [0.0123; 0.9902] 3.1195 1.7662 79.09 97.5%

Test for subgroup differences (random effects model):

Q d.f. p-value

Between groups 0.71 1 0.3981

Prediction intervals for subgroups:

95%-PI

Region = Europe [0.0607; 0.7566]

Region = Brazil [0.0000; 1.0000]

Details on meta-analytical method:

- Random intercept logistic regression model

- Maximum-likelihood estimator for tau²
- Hartung-Knapp adjustment for random effects model
- Logit transformation
- Clopper-Pearson confidence interval for individual studies



Funnel plot of substandard anabolic androgenic steroids from 8 studies

Review: Substandard

Linear regression test of funnel plot asymmetry Test result: t = -0.03, df = 6, p-value = 0.9803

Sample estimates: bias se.bias intercept se.intercept -0.7573 29.3840 -0.4926 0.3486 Details:

- multiplicative residual heterogeneity variance (tau² = 32.7035)
- predictor: inverse of total sample size
- weight: inverse variance of average event probability
- reference: Peters et al. (2006), JAMA

Meta-regression by publication year



Mixed-Effects Model (k = 8; tau² estimator: ML)

tau^2 (estimated amount of residual heterogeneity): 1.1616
tau (square root of estimated tau^2 value): 1.0778
I^2 (residual heterogeneity / unaccounted variability): 96.1925%
H^2 (unaccounted variability / sampling variability): 26.2642

Tests for Residual Heterogeneity:

Wld(df = 6) = 187.8444, p-val < .0001 LRT(df = 6) = 253.3894, p-val < .0001

Test of Moderators (coefficient 2):

F(df1 = 1, df2 = 6) = 1.9481, p-val = 0.2123

Model Results:

estimate se tval df pval ci.lb ci.ub

intrcpt -469.6791 336.1271 -1.3973 6 0.2118 -1292.1525 352.7943 Publ.Year 0.2325 0.1666 1.3957 6 0.2123 -0.1751 0.6401

----Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1